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VOLUME XXVII NUMBER 4

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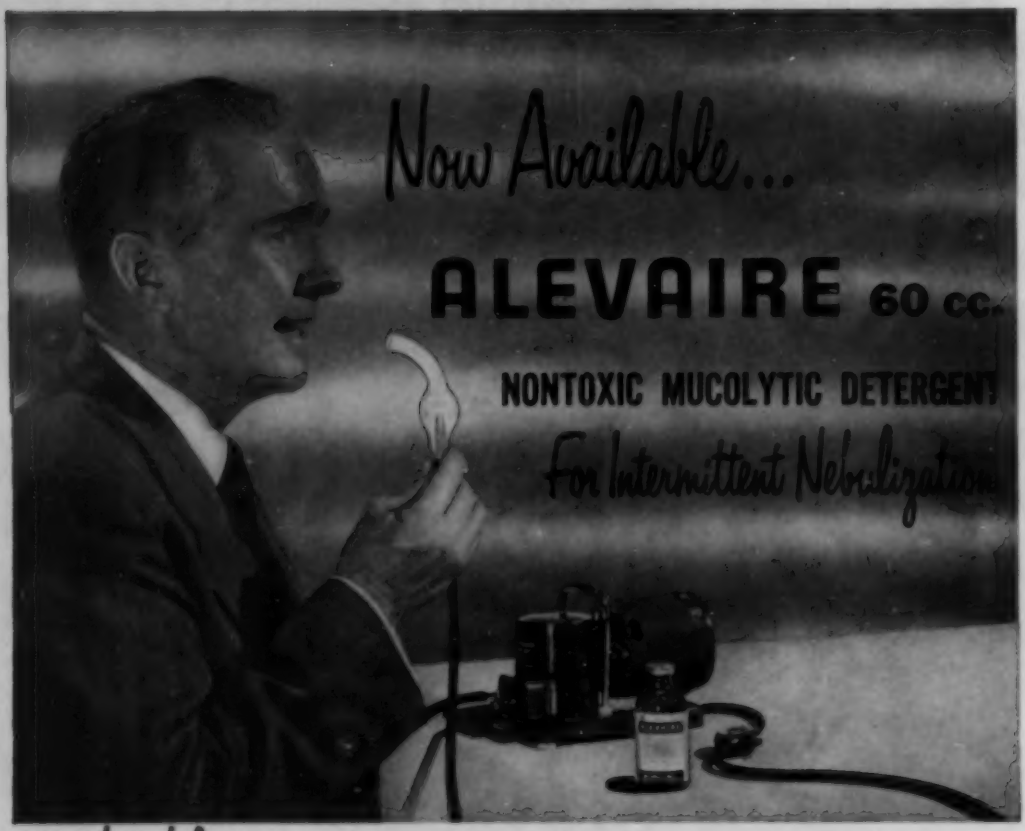

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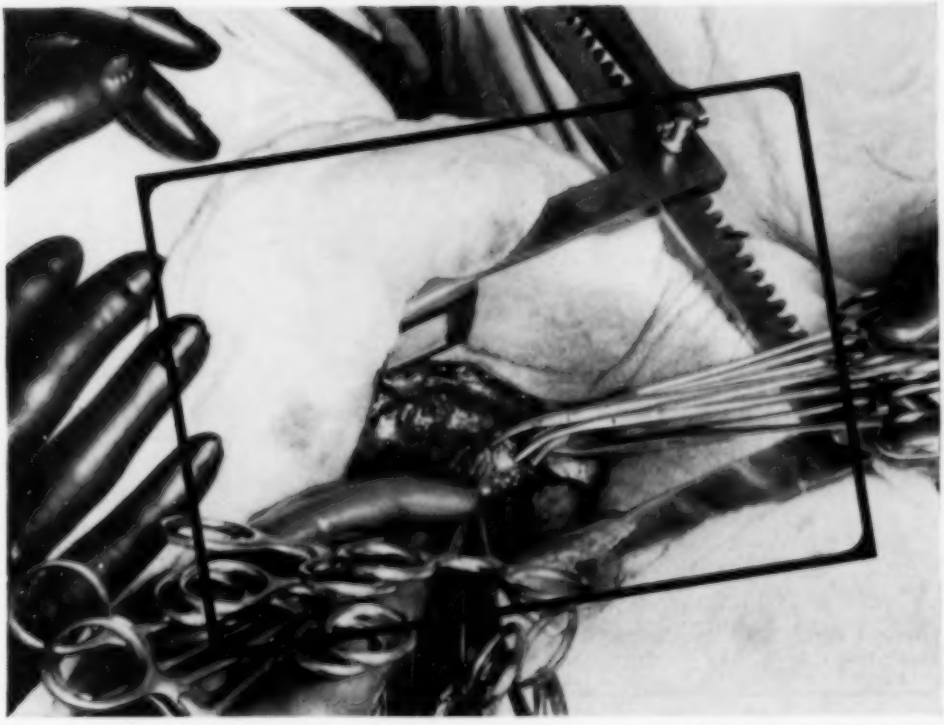

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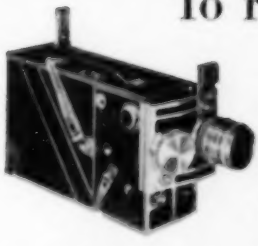

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DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

EXECUTIVE OFFICE

112 East Chestnut Street, Chicago 11, Illinois

MURRAY KORNFELD, *Managing Editor*

VOLUME XXVII APRIL, 1955 NUMBER 4

SPECIAL ISSUE ON CARCINOMA OF THE LUNG

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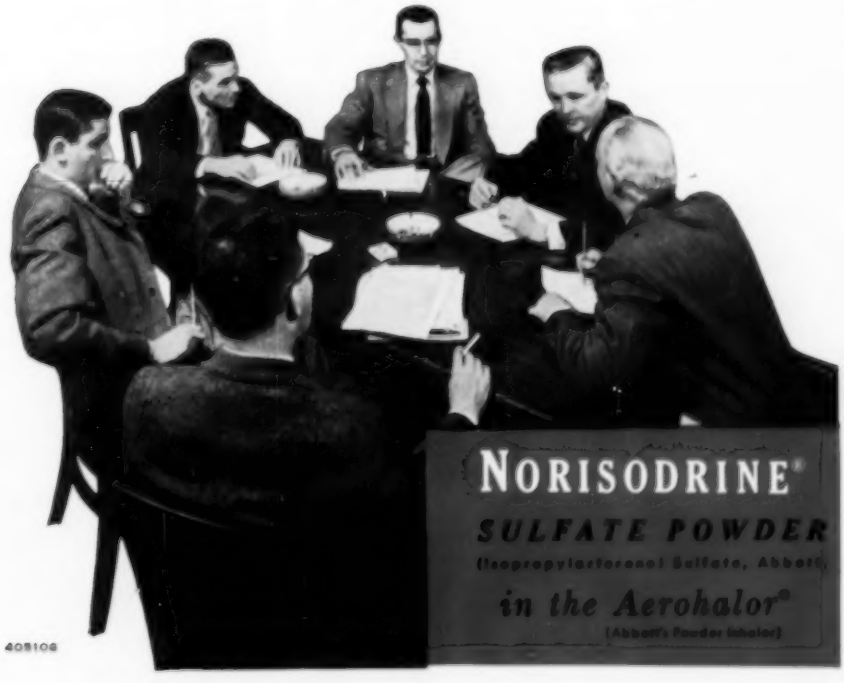

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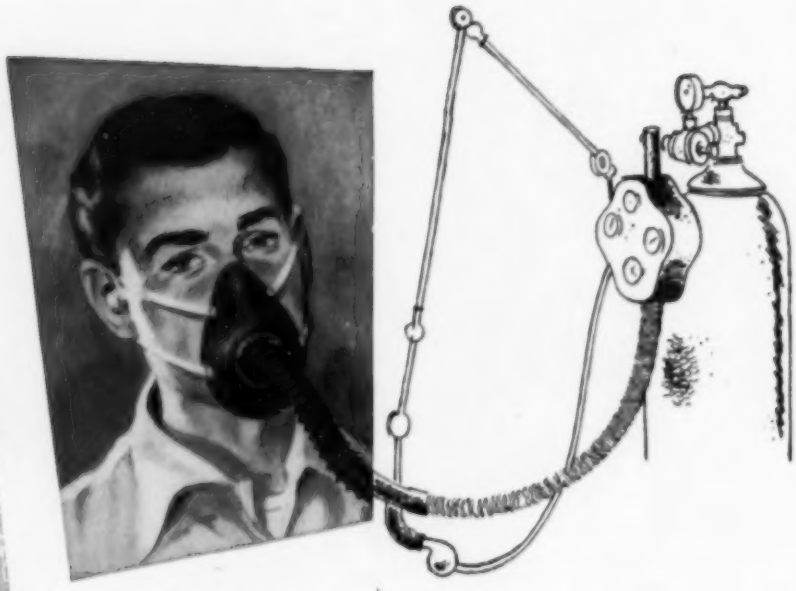

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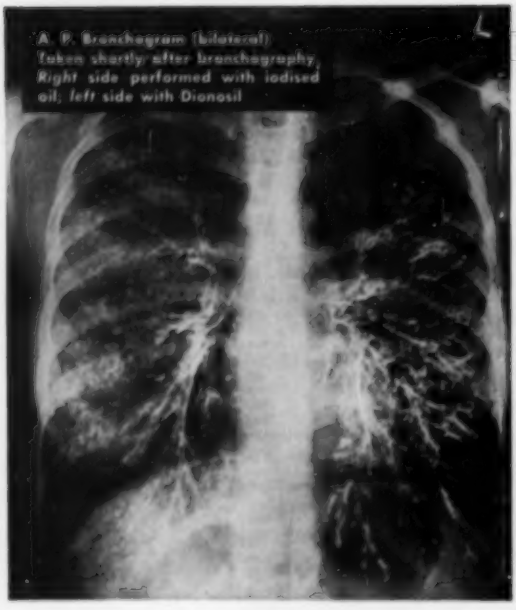

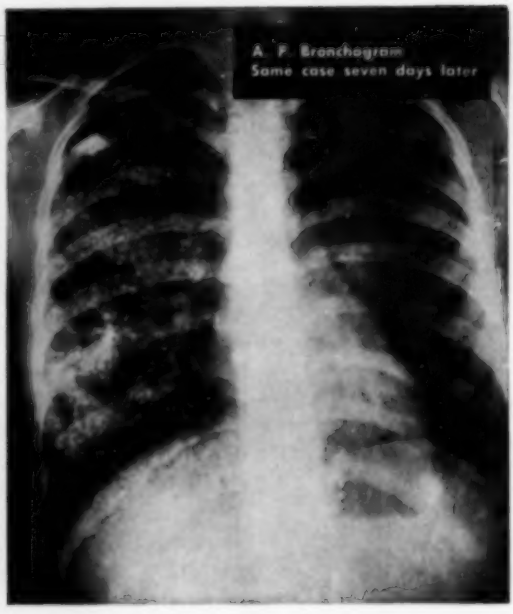

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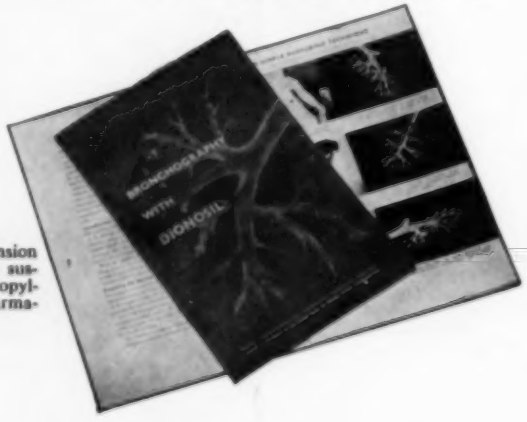

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DISEASES of the CHEST

VOLUME XXVII APRIL, 1955 NUMBER 4

A Brief Discussion of the Etiology of Bronchiogenic Carcinoma

EVARTS A. GRAHAM, M.D., F.C.C.P.
St. Louis, Missouri

It is a high honor which I greatly appreciate to be invited to give the first Jacob Jesse Singer lecture before the American College of Chest Physicians. A close association of approximately 20 years with him gave me the opportunity to recognize his many fine qualities. It was a great shock to me when I received the news that he had been suddenly struck down a few months ago. However, his friends can all be glad that before his death he knew that this lectureship had been established in his honor.

My first acquaintance with him was in the fall of 1919 after my discharge from the army when I went to St. Louis to become the Bixby Professor of Surgery at Washington University. My interest in the future possibilities of chest surgery had been aroused by my connection with the Empyema Commission during World War I. I found Jack to be greatly interested in what we had done and to be particularly well acquainted with the experimental work on pneumothorax which Bell and I had carried out while members of the Commission. He had already begun to specialize in the diagnosis and medical treatment of chest diseases and we naturally fell together as a sort of sympathetic team.

Soon it became evident that it would be desirable for us to have some space in the Barnes Hospital where we could examine patients with a fluoroscope and have daily conferences with each other, with members of the house staff and with such students as cared to attend. We began in some old storage quarters on the second floor which Jack persuaded the superintendent to let us have. We installed a fluoroscope and other equipment and began functioning in the fall of 1920 as a so-called Chest Service. Our conferences became daily occurrences every afternoon—at first for about an hour, and later becoming lengthened to two or three hours. Almost at once we were faced with the problem of an inability to accommodate the number of visitors who wanted to come—not only students and others from our own institutions but from out of town as well.

It was a great personal loss to me when Jack made the decision to go to Los Angeles but fortunately we were able to keep up our friendship

From the Department of Surgery, Washington University School of Medicine and Barnes Hospital, St. Louis, Missouri.
Emeritus Bixby Professor of Surgery, Washington University, St. Louis.
First Jacob J. Singer Lecture delivered under auspices of American College of Chest Physicians, San Francisco, June 7, 1954.

by correspondence and by seeing each other at meetings of the American Association for Thoracic Surgery of which he was a long-time and much interested member.

During the days of high mortalities in chest surgery it was a great comfort to me to have Jack's support. At times also he put the brakes on me. The conservatism which he expressed on those occasions, although sometimes resented by me, was probably good for both of us. The younger chest surgeons of today cannot possibly appreciate the criticism both open and veiled which the internists had in the 1920's for those of us who were trying to develop chest surgery. It seemed to be the general opinion of the medical men that to refer a patient to a chest surgeon was the equivalent of notifying St. Peter to expect a new arrival. It required courage for Jack to give me his support during those dark days, for he undoubtedly lost caste among his confreres by doing so. I am glad to make this expression of appreciation even if it is posthumous.

Jack Singer had a gift for things mechanical. Working on his pneumothorax apparatus gave him a great thrill; and when the final model was completed he felt a great satisfaction. It was undoubtedly the most efficient and the simplest to use of any of the apparatuses of the time. His supraglottic aspiration method of using lipiodol for bronchography was a very important addition to our diagnostic armamentarium and unquestionably its invention, by supplanting more cumbersome and even dangerous methods, did much to popularize the use of bronchography.

Now to get to the subject matter of the lecture.

With the exception of a very few die-hards, who refuse to admit the evidence, almost everyone agrees that bronchiogenic cancer, or primary cancer of the lung, has shown a remarkable increase in its incidence during the last 25 years. For example, the vital statistics of the U. S. Public Health Service show that in 1930 the deaths from the condition in men were less than those from cancer of the skin, of the liver, of the rectum, the intestine, the prostate and the stomach. By 1950, however, the most recent year when the statistics are available, bronchiogenic cancer had taken first place in the cancers affecting the male sex, and, from all that is known, the increase is progressing. The incidence of most of the other cancers has shown practically a straight line during the 20 years.

This astonishing increase in the incidence of lung cancer during a short period constitutes a most remarkable phenomenon which apparently is unique in the history of cancer. It behooves everybody, therefore, who is interested in this disease to try to find an explanation.

One other remarkable fact about bronchiogenic carcinoma is that it occurs much more frequently in the male sex. There is a considerable difference in the published statistics of the sexual ratio. Probably about an average ratio would be six males to one female.

Since the rapid increase of this disorder has roughly paralleled the rapid increase in the use of motor vehicles, it was only natural to suspect that perhaps the explanation might lie in the general exposure to some possible carcinogen connected with the automobile. However, in a study of 857 cases of bronchiogenic carcinoma by Wynder and myself (1951) with

special reference to industrial exposures as possible etiological factors, we found no significant increase of this cancer in garage men, automobile mechanics, chauffeurs and oil-field workers. There are, nevertheless, certain other occupations which carry with them increased risks of developing the condition. Probably the most striking examples were brought out in the well-known studies made on the Schneeberg and Joachimsthal miners with incidences of 40 per cent and 48 per cent respectively of deaths from lung cancer in the two places. The interested reader may find an excellent review of the occurrence of the disorder among those miners in the article by Lorenz (1944). More recently the chromate industry has been found to be associated with a higher incidence of lung cancer than the general population. This association has been well described by Mancuso and Hueper (1951). However, one can hardly blame such industrial associations for the tremendous increase in incidence of the disease because of the relative insignificance of the numbers engaged in those industries. Kotin has recently discovered some carcinogens in the atmospheric smog of Los Angeles. But it would be difficult to incriminate atmospheric pollution for the widespread increase of bronchiogenic carcinoma because if that were a responsible factor women undoubtedly would be victims of the disease as often as men. Moreover, as Peacock of Glasgow has informed me, there are analyses of the atmosphere of that city which were made a century ago that show practically the same composition as today. It would seem therefore that if atmospheric pollution is an important etio-

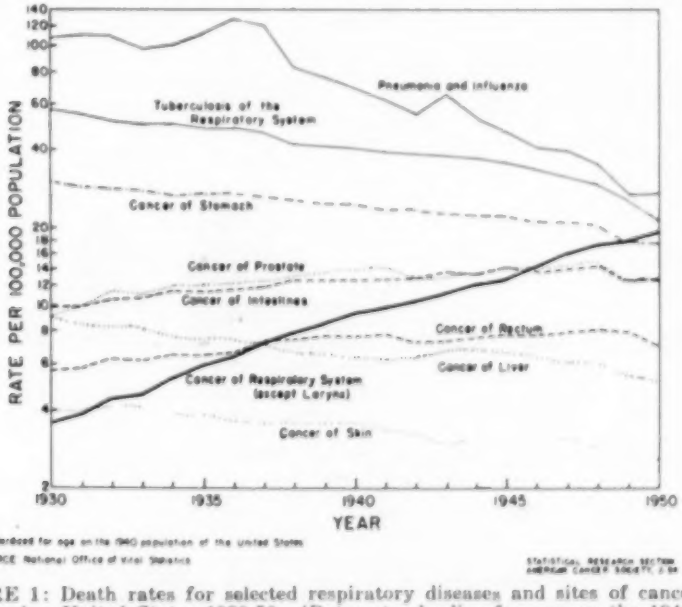

FIGURE 1: Death rates for selected respiratory diseases and sites of cancer among white males, United States 1930-50. (Rates standardize for age on the 1940 population.) The chart shows the rapid rise in the curve of incidence of cancer of the respiratory system in comparison with the nearly straight lines of other common cancers. (Prepared by Dr. E. Cuyler Hammond, chief statistician of American Cancer Society, and reproduced with his permission.)

logic factor there would not have occurred the same recent great increase in the incidence of lung cancer in Glasgow that has been noted elsewhere in Great Britain and in the United States.

Another possible etiologic factor that has been suggested frequently is tobacco smoking. This suggestion was made as long ago as 1912 by Adler who wrote the first monograph on primary lung cancer at a time when the condition was still rare. Brosch in 1900 had made some unsuccessful attempts to produce cancer experimentally in guinea pigs by painting them with tobacco "juice." The list of additional writers who since then have mentioned smoking as a possible factor is a long one. Most of them, however, were content to make the suggestion and did nothing further to find out. However, a few submitted their idea to experimental studies, but the experiments were not conducted for a long enough time and in some instances the method of study is not reported in sufficient detail to make the results satisfactory. For example, Hoffmann and his associates painted their animals (mice) for only 14 days, a very inadequate length of time, but they did observe hair loss. Wacker and Schmincke noted epithelial proliferation in rabbits' ears 21 days after a subcutaneous injection of pipe tar. Lorenz and his co-workers failed to obtain pulmonary

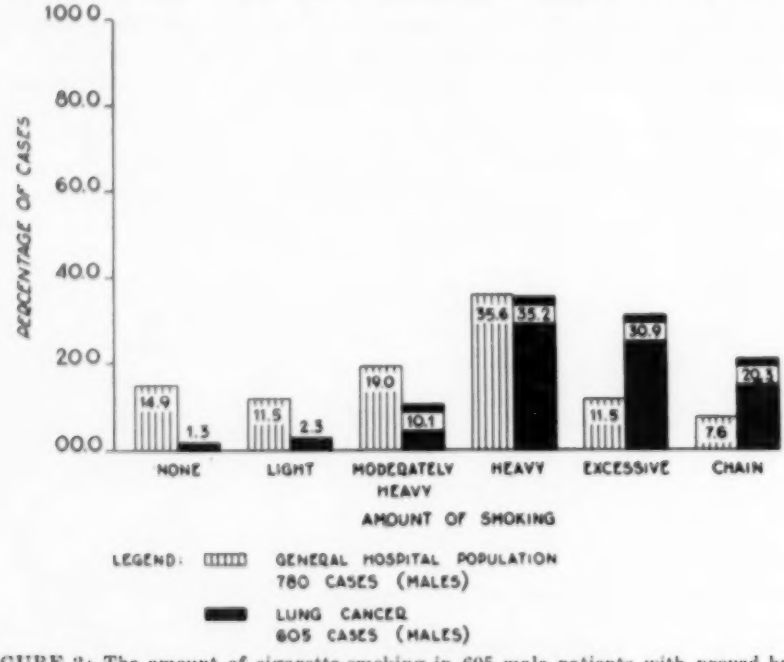

FIGURE 2: The amount of cigarette-smoking in 605 male patients with proved bronchiogenic carcinoma as compared with 780 males over 35 years of age without cancer of the lung (Wynder and Graham 1950). The arbitrary classifications of smoking are as follows: Non-smokers (less than one cigarette per day for more than 20 years); light smokers (up to one-half pack per day for more than 20 years); moderately heavy (one-half to three-quarters of a pack); heavy smokers (three quarters to a whole pack); excessive smokers (one to one and three quarters packs); chain smokers (more than one and three quarters packs).

tumors in mice which were made to inhale tobacco smoke. The literature on the attempts to produce cancer experimentally has been summarized in an article by Wynder, Graham and Croninger (1954). Ochsner and DeBakey in 1941 called attention to the similarity of the curve of the increased sales of cigarettes in this country to the greater prevalence of primary cancer of the lungs and concluded from those curves that there is a possible etiologic relationship between cigarette smoking and bronchiogenic carcinoma.

In spite of sporadic suggestions of an etiologic relationship and a few experimental attempts to produce cancer with tobacco products no large scale study was undertaken to try to determine such a possibility until 1949 when Wynder and the writer began theirs. In May, 1950, that study was published. It was based on 684 proved cases of bronchiogenic carcinoma. Nearly all the patients were in the Barnes Hospital, St. Louis, but the sampling was not restricted to a small locale since the patients came from many places in the Middle West and Southwest of the United States. They were interviewed about their smoking habits by one of two non-medical young women who used a standard questionnaire which had been devised by us. The study brought out the fact that of 605 men with bronchiogenic carcinoma, other than adenocarcinoma, no less than 86.5 per cent had smoked from about a pack to more than two packs of cigarettes a day for at least 20 years; and among those men with the two com-

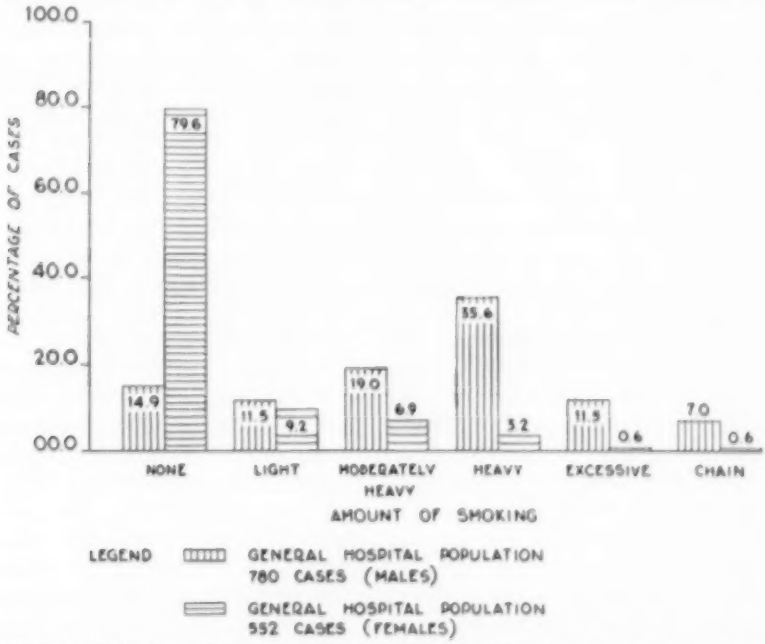

FIGURE 3: This chart shows to be false the common idea that women smoke as much as men. The statistics were obtained by questioning 780 male and 552 female patients in the Barnes Hosital. None of the patients had a bronchial carcinoma and all were more than 35 years old.

mon types of carcinoma (epidermoid and undifferentiated) only 1.3 per cent were non-smokers. Of a control group of 780 men without lung cancer 54.7 per cent had a similar history of heavy smoking of cigarettes but as many as 14.9 per cent were non-smokers. Another important finding was that no less than 72 per cent of the lung cancer patients stated that they had smoked from 30 to 50 years. Our study also showed to be erroneous the current opinion that women smoke as much as or more than men. Of 552 women patients without lung cancer and above the age of 35, in the Barnes Hospital, no less than 79.6 per cent of them were non-smokers, as compared with only 14.9 per cent of men in a similar group. It is the young women and the girls, rather than the women of the cancer age, who do the heavy smoking. Moreover, they are too young to have smoked the necessary time to develop a lung cancer, 25 years or so.

Our results were strikingly confirmed by the publication in September, 1950, of the now well-known statistical study of Doll and Hill in England. Their study was being made at the same time as ours, but we happened to precede them in publication by a few months. It was based on about the same number of patients as ours. Of 649 men with lung cancer they found only 0.3 per cent of non-smokers, compared with our figure of 1.3 per cent. As in our series Doll and Hill found that a high percentage of the men with cancer were heavy cigarette smokers. They concluded that their findings "suggest that, above the age of 45, the risk of developing the disease increases in simple proportion with the amount smoked, and that it may be approximately 50 times as great among those who smoke 25 or more cigarettes a day as among non-smokers."

In addition to our own and that of Doll and Hill there have been 10 other statistical studies reported, making 12 in all (Dungal 1950, Levin et al. 1950, Mills and Porter 1950, Schrek et al. 1950, Gsell 1951, McConnell et al. 1952, Kouloumies 1953, Sadowsky et al. 1953, Wynder and Cornfield 1953 and Breslow et al. 1954). The results of all of the 12 studies have been essentially the same. They have all shown that cancer of the lung occurs nearly always in heavy cigarette smokers. It is very significant that no study has been reported which gives any different conclusion. The skeptics should ponder that fact.

The general agreement among all the statistical studies is very strong evidence in itself that there is a definite etiologic relationship between excessive cigarette smoking and cancer of the lung. Yet obviously that relationship would seem to be more definitely established if cancer could be produced experimentally by the use of cigarette smoke. Earlier in this article brief mention has been made of a few of the experimental attempts using various tobacco products. The literature pertaining to this earlier work has been summarized in an article by Wynder, Croninger and myself published in 1953. For the most part the results have been negative, although a total of seven epidermoid cancers of the skin have been reported as having been obtained in mice with products of cigarette smoke out of many animals used. Most workers who have attempted to cause experimental cancer with tobacco products have used rabbits. Roffo (1939) reported the successful production of carcinoma in rabbit ears after paint-

ing them with a distillate of tobacco, but Sugiura failed in his attempt to reproduce Roffo's results. Also Flory (1941) succeeded in obtaining only what he called "carcinomatoids" in rabbit ears after application of a tobacco distillate.

It seemed therefore that the actual experimental production of carcinoma by the use of tobacco products had been so rare that a doubt could be raised that in any instance an etiologic relationship had been established. On the basis of that conclusion we decided to undertake some experiments to determine if cancer could be produced by the use of tar from cigarette smoke. It seemed to us highly desirable, if possible, to bring some experimental evidence to this controversial subject, in addition to the statistical evidence. An especially important point was to use a proper strain of mice which is known not to develop spontaneous cancers of the skin. In the study therefore we used the inbred strain known as CAF_1 that was developed in Dr. C. C. Little's laboratory at Bar Harbor, Maine, and that is known to be free from spontaneous tumors of the skin.

A machine was devised by which, with a small electric motor, we smoked 60 cigarettes at a time. The smoke was collected in flasks cooled by dry ice. The sudden chilling of the smoke precipitated the tar from it which was dissolved in acetone. The acetone solution was painted on the skin of the mice* three times a week, after it had been evaporated to a composition of equal parts of tar and acetone. Control mice painted with acetone alone showed no reaction of the skin whatever—not even any evidence of irritation.

Papillomas appeared in 59 per cent (26 females and 22 males) of 81 tarred CAF_1 mice. Although 8.6 per cent of the papillomas regressed, no less than 44.4 per cent (or 36 mice) developed epidermoid cancer of the skin. Sometimes there were two cancers in one mouse and in one case there were three, but in most instances only one cancer appeared in the painted area. In view of the much greater frequency of bronchiogenic carcinoma in the human male it was of special interest that among the tarred mice 25 of the cancers appeared in females and only 11 in males.

Successful transplantation of the experimentally produced cancers into normal mice was easily accomplished, and in one instance a transplantation has been carried out through more than 30 generations. Of course the importance of the successful transplantations is the positive evidence of malignancy of the growth which they demonstrate.

An observation of importance that we made in connection with the experiments was that the average time of appearance of a cancer was after 71 weeks of painting. This period of time represents a little more than one-half the average life-span of the mouse, which is ordinarily a little more than two years. This time corresponds roughly with the period of smoking required for the production of a bronchiogenic cancer in the human. For our statistical observations demonstrated that 30 to 50 years of smoking precede the appearance of a bronchiogenic carcinoma, a period roughly corresponding to one-half the life span.

*For details of the experimental work our original article (Wynder, Graham and Croninger, 1953) should be consulted.

Our experiments demonstrate beyond a possibility of doubt that cigarette smoke contains something which is carcinogenic for the skin of mice.

Is this finding of significance in relation to the question of human bronchiogenic carcinoma?

It would seem to the writer that, even when taken alone, the finding of a carcinogenic substance in cigarette smoke is of very great significance. When combined with the findings of the statistical studies the importance

FIG. 4

FIG. 5

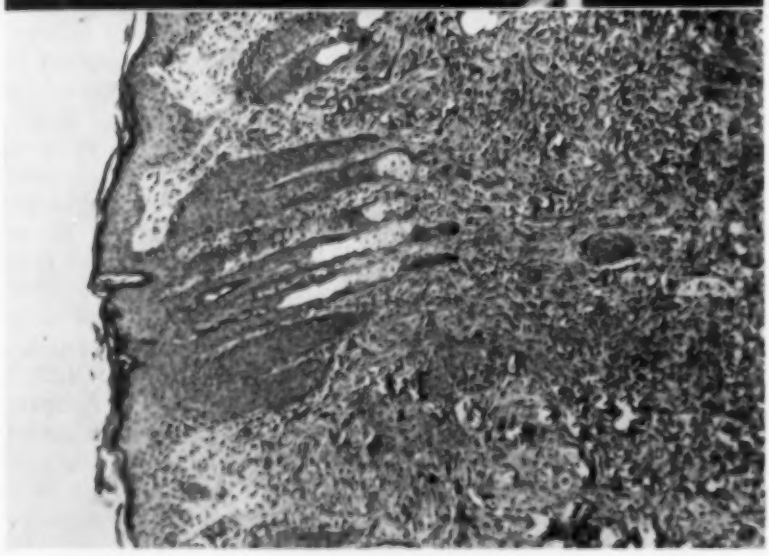

Figure 4: Beginning carcinoma after 322 days of painting with cigarette tar.—
Figure 5: Photomicrograph of same lesion at 371 days.

of these experimental observations is greatly increased. To many the fact that all the published statistical studies point in the same direction together with now the successful production of epidermoid cancer in mice by painting the skin with the tar derived from cigarette smoke makes the chain of evidence incontrovertible. Others, however—and these are usually heavy cigarette smokers—decry the significance of our experimental results. They state that no absolute proof has been produced that there is any etiologic relationship between cigarette smoking and cancer of the lung.

It must be admitted that the proof of a definite relationship does not exist. To establish such proof to the satisfaction of the "die-hards" would require human experimentation carried out on the same individuals for more than a quarter of a century. Obviously such experiments cannot be conducted. Perhaps one could say that if the agent involved in the case were something less desired by the users of it than are cigarettes by their habitués there would be no difficulty in the general acceptance of the evidence. If, for example, the findings pointed to a substance like spinach as the guilty party instead of the habit-forming cigarette, would there be as much difficulty in accepting the evidence?

By many of the writers on this subject there is too much of a tendency to consider bronchiogenic carcinoma as if it were one disease. On the contrary there is much evidence to indicate that there are several varieties which are so different from each other that probably they represent actually different diseases. At least three varieties can be easily distinguished with different etiologies. The fact that smoking is not a causative factor in at least two of the three varieties leads to confusion in the minds of some observers who are not aware of the differences because, as they state, they can cite cases in which the patients never smoked.

The three varieties which seem to me to be clearly distinguishable from each other are:

(1) The epidermoid or squamous cell. Sometimes the structure of this tumor is not clearly differentiated, and for that reason I like to include in this group the so-called "undifferentiated" cancers. This group is the common bronchiogenic carcinoma which in our experience constitutes well over 90 per cent of all bronchial cancers. At the present time it occurs much more commonly in the male. It is found very rarely in a non-smoker. It is this variety of lung cancer which has shown the very striking increase in incidence.

(2) The adenocarcinoma. When typical this tumor has several characteristics which set it apart from the epidermoid cancer. For one thing, our statistical studies showed that it has a much less close relationship to smoking. In our series, out of 39 men with adenocarcinoma no fewer than four (10 per cent) were non-smokers, whereas among the other 605 men with bronchiogenic carcinoma the proportion of non-smokers was only 1.3 per cent. Even more remarkable was the fact that of 15 women with adenocarcinoma 13 were non-smokers. Another characteristic of the adenocarcinoma which distinguishes it from the epidermoid variety is that it occurs with about equal frequency in the two sexes. Again, the adenocarcinoma has a special tendency to involve younger people; or, to put it

in another way, whenever a young person has a bronchiogenic carcinoma it is nearly always an adenocarcinoma. Olson (1935) states of 576 cases of lung cancer compiled from the literature by Brunn in 1926, 12 per cent were in the age group 20-29, and all of them were adenocarcinoma. These characteristics seem to set off this tumor from the more common epidermoid cancer and to suggest that it is a different disease entity with a different etiology. Perhaps in at least some cases the adenocarcinoma has had

FIG. 6

FIG. 7

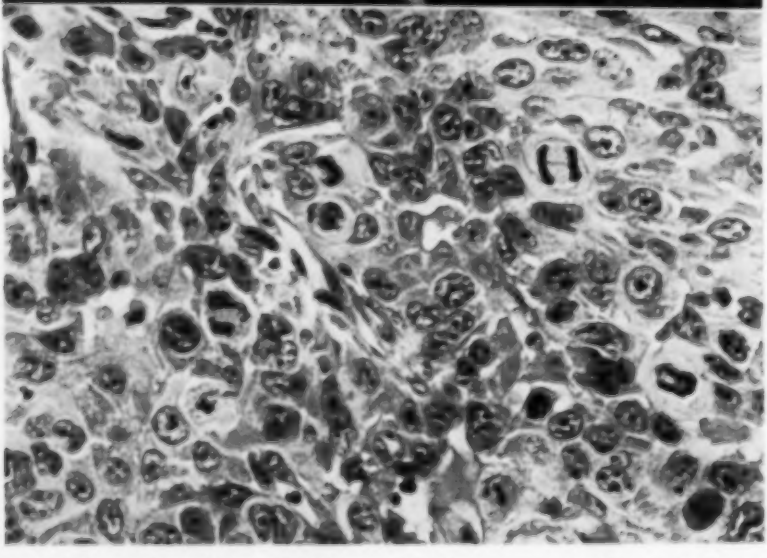

Figure 6: Advanced carcinoma (2 lesions) in another mouse at 590 rays of painting.—*Figure 7:* Photomicrograph of lesion at left.

its origin in a so-called bronchial adenoma which has become malignant. In 1938 Womack and I presented evidence that the so-called bronchial adenoma is a potentially malignant tumor capable of producing both regional and distant metastases. Such an idea at that time was not generally accepted but there are few who oppose it now. A common microscopic pattern seen when the tumor has become malignant is that of an adenocarcinoma. It would seem reasonable to conclude therefore that at least some of the adenocarcinomas have arisen in bronchial adenomas.

(3) The so-called alveolar-cell carcinoma. This type is rare compared with the other two types. Both the gross appearance of the involved lung and the microscopic characteristics of the tumor resemble very closely the disease of sheep known by the South African word, "jagziekte." It is probably due to a virus.

[Note: Some of the text and illustrations appearing in this article were previously published in my Sir John Fraser Lecture, delivered at the University of Edinburgh, May 11, 1954, and printed in *Lancet* of June 26, 1954, pp. 1305-1308. This material is reproduced here with the permission of the editor of *Lancet*.]

CONCLUSIONS

(1) A very remarkable increase in the incidence of bronchiogenic carcinoma has occurred in the last 25 years. From having been a curiosity in 1930, by 1950 it was so common that it had become the most frequent cancer in the male sex.

(2) No less than 12 statistical studies have shown a definite etiologic relationship between the disease and excessive cigarette smoking. Of equal importance, perhaps, is the fact that no careful study has been published which fails to show that relationship.

(3) The statistical evidence has been strongly supported by the experimental production of epidermoid carcinoma in the skin of CAF_1 mice by painting the skin with tar obtained from cigarette smoke. The incidence of cancer production was 44.4 per cent in 81 tarred mice.

(4) A mistake is commonly made in thinking that bronchiogenic carcinoma is a single disease. Actually there seem to be at least three separate varieties with different etiologies.

RESUMEN

1. En los últimos 25 años ha habido un notable aumento en la frecuencia del carcinoma bronquigénico. Siendo una curiosidad en 1930, ya en 1950 es tan común que se ha convertido en el cáncer más frecuente en el sexo masculino.

2. No menos de doce estudios estadísticos han demostrado de finidamente una relación etiológica entre la enfermedad y el fumar excesivo. De igual importancia quizás, es el hecho de que no se ha ya publicado un estudio cuidadoso que deje de mostrar esa relación.

3. La evidencia estadística es soportada fuertemente por la producción experimental del carcinoma epidermoide de la piel de los ratones CAF por medio de las embrocaciones de la piel con el alquitrán obtenido del humo de cigarrillos. La incidencia de la producción del cáncer fué de 44.4 por ciento en 81 ratones alquitranados.

4. Es un error común el considerar que el carcinoma bronquiogénico es una sola enfermedad. De hecho parece que hay cuando menos tres diversas variedades con etiologías diversas.

RESUME

1. Dans les 25 dernières années, on a noté une augmentation très importante de la fréquence du cancer bronchique. Considéré comme une curiosité en 1930 il átait si répandu en 1950 qu'on pouvait le considérer comme le cancer le plus fréquent dans le sexe masculin.

2. Douze études statistiques au moins ont montré une relation étiologique incontestable entre cette affection et la consommation excessive de cigarettes. Peut-être faut-il attacher la même importance au fait qu'aucune étude attentive n'a été publiée concernant les cas où cette relation n'a pu être mise en évidence.

3. Les constatations statistiques ont été renforcées solidement par la production de cancers épidermoídes sur la peau de souris après application de goudron extrait de la fumée de cigarette. Sur 81 souris ainsi préparées, il y eut 44,4% de cancer.

4. C'est une erreur commune de penser que le cancer bronchique est une maladie simple. Actuellement, il semble qu'il y a au moins trois variétés différentes de cancer avec des étiologies diverses.

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Is Survey Cancer of the Lung Curable?

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Lung cancer has increased precipitously in the last 30 years. The increase can probably be estimated by the trend in death rates, so closely does morbidity approach mortality. While a few thoracic surgeons are sanguine about their results, the over-all five year survival rates continue to be under 10 per cent. Is this disease curable—or would it be if we could detect it earlier? By what means is early detection possible? Some authors suggest that chest x-ray surveys are an answer.[1,2,3,4]

Since the official Philadelphia Chest Survey Program has been as interested in detecting lung cancer as in finding active tuberculosis, it seems appropriate to examine the survival rates of survey cancer patients. In 1949, through following survey cases suspected of having tuberculosis, it became evident that lung cancer was masquerading as tuberculosis. Therefore, policy was inaugurated for reporting as "Suspect Neoplasm" all abnormalities for which this seemed a possible diagnosis. Liaison with hospitals is excellent so that diagnostic studies may be promptly obtained. In addition, there is meticulous follow-up of all persons with abnormal photofluorograms. The fate of primary bronchogenic carcinoma cases detected at these units may help illuminate the role of surveys in finding curable lung cancer.

Materials and Methods

The prevalence of persons classified as "Suspect Neoplasm" was examined because the promptness of resection is related to the index of suspicion.

The prevalence of proved cancer cases was studied by age, race, and sex among 142,156 persons on whom appropriate basic data were available. Sixty-three per cent of these persons were foodhandlers required by law to have annual chest roentgenograms.

A list was made of 100 consecutive carcinoma cases detected at two official Philadelphia City Chest X-ray Units beginning with January, 1947. Only those were included whose diagnoses were confirmed pathologically by tissue obtained at operation, by biopsy and by autopsy. In eight instances in which the clinical course and roentgenographic changes on serial films were consistent, positive cytologic reports on bronchial secretions were accepted as proof.

Resectability and survival rates were studied and correlated with age, race, sex, photofluorographic appearance, presence or absence of symptoms at the time of the first photofluorogram recognized as abnormal, broncho-

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scopic appearance, bronchoscopic biopsy, cytologic reports on bronchial secretions and tissue diagnoses.

Detailed survival studies were limited to three-year survival rates on 57 persons whose first abnormal photofluorograms had been taken at least three years before the close of the study.

Concomitant tuberculosis was studied. Only those cases were accepted as active tuberculosis in whom the clinical diagnosis was substantiated by more than one positive sputum. In two instances the coexistence of tuberculosis was found by post mortem examination.

Patients were divided into two categories—58 "preclinical" who had not sought medical advice prior to the time of the first recognized abnormal photofluorogram and 42 "clinically manifest" who had consulted physicians because of respiratory symptoms. The "preclinical" patients were further subdivided into 10 who were truly asymptomatic and 48 who, on careful questioning, were found to have respiratory symptoms.

A study was made of the interval between the first abnormal photofluorogram and the hospitalization resulting in the diagnosis of carcinoma. When hospitalization had been effected within one week, it was considered there had been no delay. The total delay period was broken down according to the following components: delay attributable to (1) radiologist, (2) administration, (3) clinician, (4) patient, and (5) difficulty in obtaining hospital beds.

Radiological delay was limited to those delays which had deferred referral to a clinician. If the photofluorographic reading had been such that the patient had been expeditiously referred even though the radiologist had not suspected neoplasm, delay was not attributed to the radiologist since surveys are screening processes, not diagnostic in nature. It seemed fair to assume that, if a patient was hurried to a clinician because of an abnormal film, it was the clinician's responsibility to proceed as rapidly as possible to the definitive diagnosis.

In 29 instances, earlier photofluorograms were available for retrospective review.

In connection with the 81 deaths, the median interval was studied between the abnormal photofluorogram and death for the various factors suspected of having prognostic significance.

Follow-up was closed as of August 31, 1953, yielding data on a period of three to 80 months.

RESULTS

Prevalence of Photofluorograms Suggesting Neoplasm

As follow-up experience was correlated with photofluorographic readings, the rate per 100,000 of photofluorograms read as "suspect neoplasm" increased from 135 in 1949 to 219 in 1953. The rate for men over 45 was 556. Guiss[3] reported that 190/100,000 photofluorograms were interpreted as suggesting neoplasm in the 1950 Los Angeles Survey in which 1,867,201 persons were x-rayed.

Of 607 persons at all ages whose photofluorograms were interpreted as "suspect neoplasm," 10 per cent were proved to have bronchogenic carci-

noma. Of the men over 45 years of age with such readings, 18 per cent had lung cancer.

Prevalence rates of proved primary cancer per 100,000 persons surveyed were 37 for the whole group of 142,156, three for females, and 69 for males. For males over 45, the rate was 284 (Table I) (Figure 1). There was no significant difference between whites and non-whites. The prevalence of proved lung cancer in the Boston survey was only 7/100,000[5]. This low prevalence is not due to basic differences between the Boston and Philadelphia surveyed populations since the Philadelphia group was younger and had fewer males over 45 than had the Boston group.

Resectability

Resectability is essential to survival. However, it is no end in itself. The anguish and expense of surgery are only meaningful when cures are obtained. Therefore, resectability rates are of interest but the vital figures are on those resected who have survived for significant periods of time.

Of the 100 cases, 52 were explored but only 30 were resected, a rate slightly below that reported by Gibbon et al[6] and McDonald[7] but higher

TABLE I

PREVALENCE OF PROVED BRONCHOGENIC CARCINOMA AMONG INDIVIDUALS REFERRED TO TWO OFFICIAL PHILADELPHIA UNITS* BY AGE, RACE AND SEX

Under 45	Number	Subtotals	Proved Bron. Ca.	Subtotal Bron. Ca.	Rate / 100,000
Male White	26,913		1		4
Male Non-White	29,200		2		7
All Males Under 45		56,116		3	5
Female White	30,495		1		3
Female Non-White	28,110		—		—
All Females Under 45		58,605		1	2
Over-all Total Under 45	114,721		4		3
Over 45	**Number**	**Subtotals**	**Proved Bron. Ca.**	**Subtotal Bron. Ca.**	**Rate / 100,000**
Male White	12,076		27		224
Male Non-White	4,501		20		444
All Males Over 45		16,577		47	284
Female White	7,809		1		13
Female Non-White	3,049		—		—
All Females Over 45		10,858		1	9
Over-all Total Over 45	27,435		48		175
Over-all Total	142,156	142,156	52	52	37
Total Males	72,693		50		69
Total Females	69,463		2		3

*Unit 1—Total 1947, foodhandlers only 1949 through 1952.
Unit 3—Total 1949 through 1952.

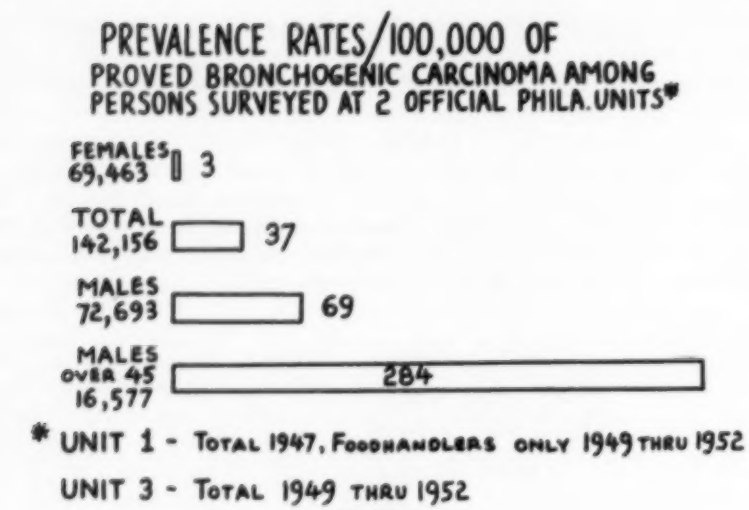

FIGURE 1

than that reported by most thoracic surgeons. When it is considered that the 52 explorations were undertaken at 18 different hospitals, the resectability rate of 30 per cent seems quite good.

Nothing striking was found in correlating resectability with age, race, sex, photofluorographic classification or clinical status. However, as in all reported series, there was a higher resectability for those with squamous cell carcinoma (Table II).

TABLE II
RESECTABILITY ACCORDING TO TISSUE DIAGNOSIS

Tissue Diagnosis	Number	Number Resected	Per Cent Resected
Squamous	59	22	37
Adenocarcinoma	16	4	25
Undifferentiated	19	4	21
Unclassified	6	—	—
Total	100	30	30

Fifteen patients were never bronchoscoped. Their diagnoses were made by autopsy in 12 and by biopsy in three instances. Reports are not yet available on two patients. Twice as high a percentage of the 21 patients with grossly normal bronchoscopic findings were resected as of the 62 with any abnormal findings at all (Table III). The gross bronchoscopic findings were as follows:

GROSS FINDINGS ON 81 CANCER CASES*

Normal	21	Stenosis	2
Tumors visualized	27	Bloody Secretion	8
Compression or Distortion	20	Mucosal Thickening	3**
		Excessive Secretions	4

*Categories not mutually exclusive
**Biopsies positive

Twenty-one had positive cytologic reports. A third of these were resected. One-fifth of the 28 with positive bronchoscopic biopsies were resected (Table III).

TABLE III
RESECTABILITY ACCORDING TO BRONCHOSCOPIC FINDINGS

	Number	Number Resected	Per Cent Resected
Not Bronchoscoped	15	—	—
Bronchoscoped*	85	30	35
Total	100	30	30
Gross Bronchoscopic Findings			
Normal	21	12	57
Abnormal	62	18	29
*Microscopic Findings***			
Positive Cytology	21	7	33
Positive Biopsy	28	6	21

*Reports not available on 2
**Categories not mutually exclusive

Over-all Survival

There are 19 survivors out of the group of 100. Fourteen of the survivors have been resected. Because of the variable length of follow-up, survival was studied by the life table method (Tables IV, V, and VI) as well as by direct observation (Figure 2). Survival rates were very close to each other by both methods.

Half the patients with survey-detected lung cancer died within the first year of their abnormal films (Table IV) (Figure 2). In our experience the chance of a survey-detected case being resected and living five years is about 10 per cent (Table V). We do not believe it is sound to dwell on the figures restricted to resected cases only. The opportunity for resection is too rare.

TABLE IV
SURVIVAL OF PROVED CASES OF BRONCHOGENIC CARCINOMA BY YEARS AFTER ABNORMAL PHOTOFLUOROGRAM*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent
0-1	100	49	8	.49	100.
1-2	43	16	2	.62	49.
2-3	25	10	4	.57	30.
3-4	11	3	1	.71	17.
4-5	7	3	—	.57	12.
5-6	4	—	4	—	**

*Computed by the Life Table Method using the equation: $p_x = \frac{d_x}{O_x - \frac{W_x}{2}}$

**Numbers too small for percentage estimation.

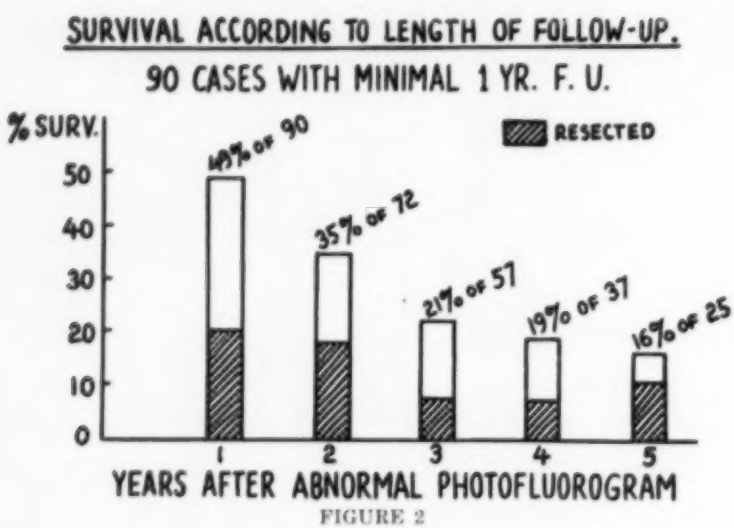

FIGURE 2

Hospital mortality was 17 per cent for the 52 thoracotomies. Five (23 per cent) died of the 22 explored but not resected and four (13 per cent) died of the 30 resected. Of the 26 who survived resection, nine died within the first postoperative year. The longest interval between the abnormal photofluorogram and death in an unresected case has been five years, one month.

Of the 57 persons on whom three-year survival rates could be calculated, 12 (21 per cent) survived three years. Only five of these have been resected, so that ultimate survival cannot be better than the dismal figure of nine per cent. The three-year survival rate for the 39 Boston cases is 13 per cent[5]. Where the prognosis is so poor, it is difficult to decide what factors are related to prognosis. The following factors were studied in an attempt to find some guides for case-finding efforts.

TABLE V
SURVIVAL OF RESECTED CASES IN YEARS AFTER FIRST ABNORMAL PHOTOFLUOROGRAM*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent	Proportion Resected and Alive**
0-1	30	6	7	.77	100.	30.
1-2	17	5	—	.71	77.	23.
2-3	12	4	4	.60	55.	16.
3-4	4	1	—	**	33.	9.6
4-5	3	—	—	**	**	**
5-6	3	—	3	**	—	—

*Computed by the Life Table Method using the equation: $q_x = \frac{d_x}{O_x - W_x - \frac{x}{2}}$

**Numbers too small for percentage estimation.

Survival According to Age, Race and Sex

Bronchogenic carcinoma may be more malignant in younger persons. Of the 21 younger than 55 on whom three-year survival studies could be

TABLE VI

SURVIVAL OF UNRESECTED CASES IN YEARS AFTER FIRST ABNORMAL PHOTOFLUOROGRAM*

Years After Abnormal Photofluorogram	Total Persons Living	Deaths	Withdrawals from Observation	Proportion Living	Survival Rate Per Cent	Proportion Resected and Alive**
0-1	70	43	1	.32	100.	70.
1-2	26	11	2	.56	32.	22.
2-3	13	6	—	.54	18.	12.
3-4	7	2	1	.69	10.	6.
4-5	4	3	—	**	7.	4.
5-6	1	—	1	**	**	**

*Computed by the Life Table Method using the equation: $p_x = \frac{d_x}{O_x - \frac{W_x}{2}}$

**Numbers too small for percentage estimation.

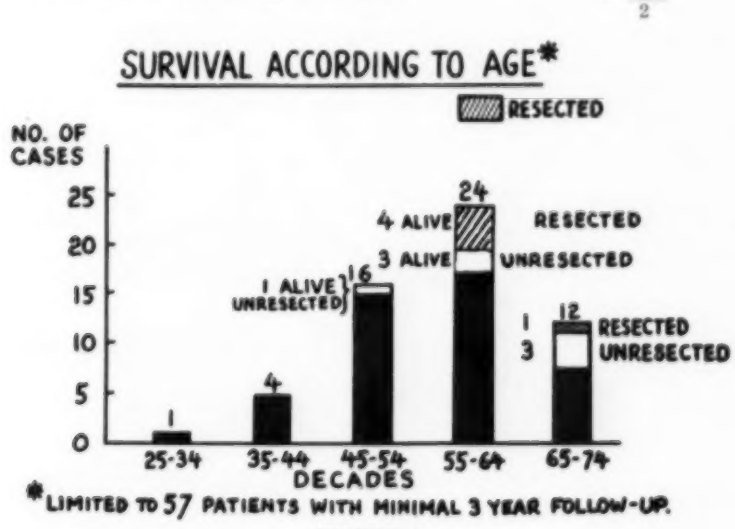

FIGURE 3

TABLE VII

SURVIVAL ACCORDING TO AGE

Age Groups Years	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
30-34	1	—	—	—	—
35-44	4	—	—	—	—
45-54	16	1	6	—	—
55-64	24	7	29	4	17
65-74	12	4	33	1	8
Total	57	12	21	5	9

calculated, only one survived three years and she died shortly thereafter (Table VII) (Figure 3). The poorer prognosis of younger persons was not due to a low index of suspicion because, among the 57 with a minimal three-year follow-up, the median delay in hospitalization was 2½ months less (207 days) for those under 55 than for those over 55 (283 days).

Another indication that lung cancer may be more malignant for younger persons is the shorter median survival time for those who died. In the over-all series, the figures were six months for the deaths in those younger than 45 compared with 10 months for those 65 to 74 (Figure 4).

There was no significant difference in survival between whites and non-whites.

Survival According to Photofluorographic Appearance

The three-year survival rate of those whose films were interpreted as "Tuberculosis" was 24 per cent (Table VIII) in contrast to the rate of 33 per cent for the "erroneous negatives".

TABLE VIII
THREE YEAR SURVIVAL ACCORDING TO PHOTOFLUOROGRAPHIC APPEARANCE

Photofluorographic Classification	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Suspect Neoplasm	21	2	10	1	5
Tuberculosis Only	17	4*	24	1	6
Suspect	4	1	**	1	**
Erroneous Negative	15	5	33	2	13
Total	57	12	21	5	9

*Three of these 4 died within the next 2 years. The sole survivor is unresected.
**Numbers too small for percentage estimation.

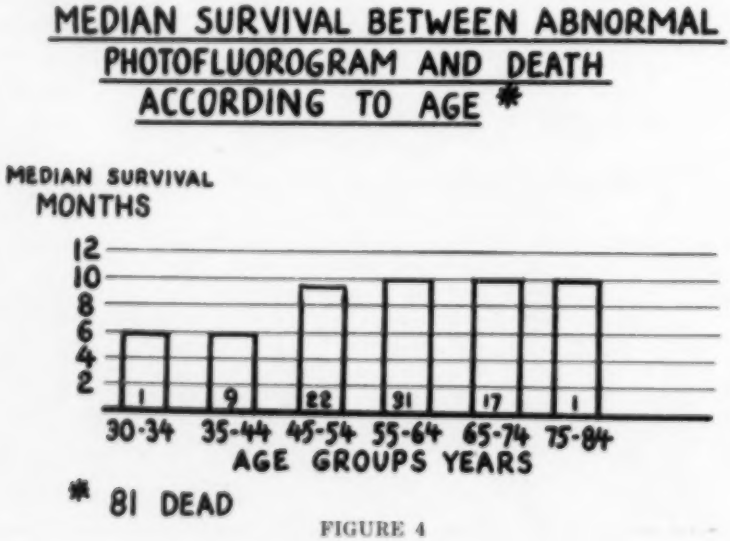

FIGURE 4

For the over-all series of 100, the median length of survival between the abnormal film and death was seven months for the 39 "suspect neoplasm" cases, 8.5 months for the 26 "tuberculosis" cases, 11 months for the 5 "suspect" cases and 30 months for the 11 erroneous negatives (Figure 5).

Survival According to Clinical Status

The presence or absence of symptoms at the time of discovery was of prognostic importance. There were only 10 asymptomatic patients in the series of 100. Four of these lived for more than three years while only one survived three years of the 19 whose symptoms had led them to seek medical advice (Table IX). Had these patients been admitted promptly

TABLE IX

THREE YEAR SURVIVAL ACCORDING TO CLINICAL STATUS AT TIME OF INITIAL PHOTOFLUOROGRAM

Clinical Status	Number	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
"Preclinical"					
Asymptomatic	10	4	40	2	20
Symptomatic	28	7	25	2	7
Clinically Manifest	19	1	5	1	5
Total	57	12	21	5	9

for diagnostic study instead of having been referred for survey films, perhaps their prognosis would have been better. When a patient seeks medical advice because of symptoms, he is likely to cooperate in carrying out the advice given.

The fate of the "preclinical" symptomatic group was better than that for those with manifest symptoms, 25 per cent having survived three years.

Survival According to Bronchoscopic Findings: Macroscopic

Bronchoscopic reports were available on 83 of the 100 patients (Table III). For the 64 dead among these 83 patients, the median interval between the abnormal film and death was 8.5 months for the 50 with

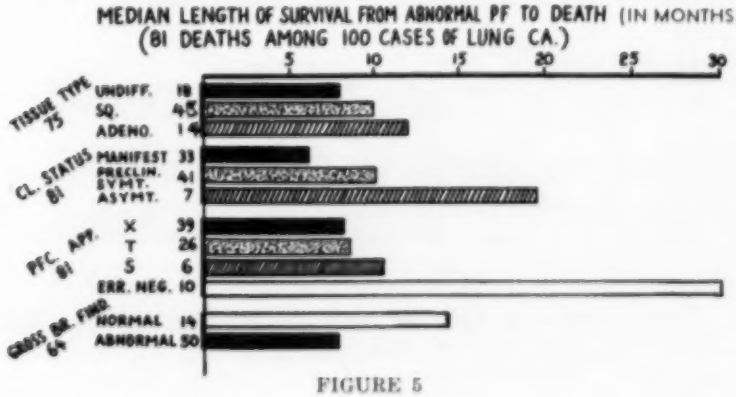

FIGURE 5

abnormal bronchoscopic findings compared to 14.5 months for the 14 with normal findings (Figure 4).

Of the 57 with a minimal follow-up period of three years, 45 had bronchoscopic reports. When any gross abnormality had been visualized, there was only a 19 per cent three-year survival. When no abnormality had been seen, the prognosis was better, 29 per cent having survived. A clearer picture is seen if one considers only the survivors who have been resected (Table X) (Figure 6).

Survival According to Bronchoscopic Findings: Microscopic

Of the 100 cases, there were 21 with positive cytologic reports and 28 with positive bronchoscopic biopsies. Only one survived five years after his abnormal film.

The findings we report are based on a group of patients selected because

TABLE X
THREE YEAR SURVIVAL ACCORDING TO GROSS BRONCHOSCOPIC FINDINGS

	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Not Bronchoscoped	12	2*	17	—	—
Normal	14	4	29	3**	21
Abnormal	31	6	19	2	7
Total	57	12	21	5	9

*Died within the next two years.
**Living and well more than five years after abnormal photofluorograms.

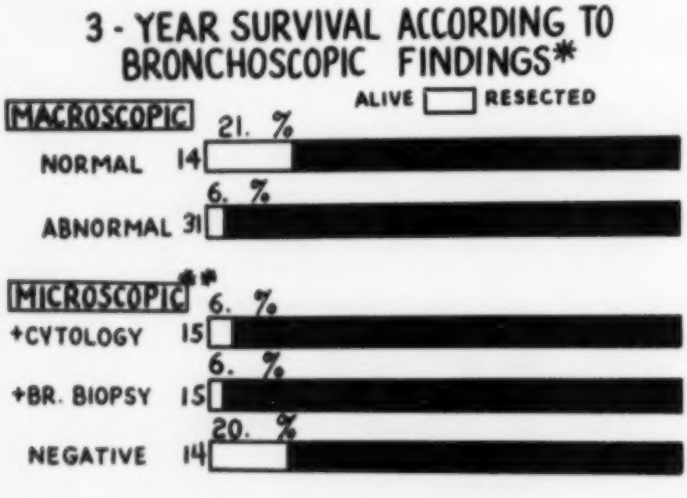

FIGURE 6

of photofluorographic abnormality. If we included patients with symptoms but negative roentgenograms and positive bronchoscopic findings, the results might be better.

Survival According to Tissue Diagnoses

The prognosis as in all reported series, was poorest for those with undifferentiated cancers (Table XI). In the series of 100, the median

TABLE XI
THREE YEAR SURVIVAL ACCORDING TO TISSUE DIAGNOSIS

Tissue Type	Number of Cases	Number Alive	Per Cent Alive	Resected and Alive	
				Number	Per Cent
Squamous Cell	35	9	26	4	11
Adenocarcinoma	10	2	20	1	10
Undifferentiated	11	1	9	—	—
Unclassified	1	—	—	—	—
Total	57	12	27	5	9

length of survival corroborates the grave outlook for those with undifferentiated carcinomas. The figures were eight months for the 18 with undifferentiated cancers, 10 months for the 43 with squamous cell carcinomas and 11 months for the 14 with adenocarcinomas (Figure 5).

Tuberculosis and Carcinoma

Ten of the 100 carcinoma patients had concomitant active pulmonary tuberculosis. None survived. It has been repeatedly pointed out that there is a real danger in failing to consider the increasing association of these two diseases in older men[8,9,10,11]. Even when multiple positive sputa confirmed by culture prove the diagnosis of active tuberculosis, radiologic evidence of tumor should indicate exploration in men over 45.

A typical case illustrating the coexistence of these diseases is F.B., a 57 year old Negro caretaker who had a photofluorogram on July 26, 1948, read as "moderately advanced tuberculosis of indeterminate activity" because of infiltrations at the left apex and in the right midlung (Figure 7). He was promptly referred to a City Chest Clinic where he was checked and rechecked in an attempt to establish a diagnosis of active tuberculosis. Because his sputum was consistently negative, the survey physician reviewed the clinic film of February 9, 1949 and at once recognized it as suspicious of neoplasm. In retrospect, obstructive emphysema on the right was visible in the film of July 26, 1948. The patient was hospitalized for bronchoscopy. Because the bronchoscopic report did not mention cancer but stated only "bronchoscopy revealed slight medial compression of the right main bronchus just below the carina," the clinic continued to carry the patient as a case of tuberculosis. They obtained a positive sputum October 20, 1948. In January of 1950, the patient was so ill that he went on his own to the Temple University Hospital for admission. Bronchial secretions were positive for tubercle bacilli but, despite this, he was explored February 21, 1950. He was found to be inoperable. Biopsy revealed

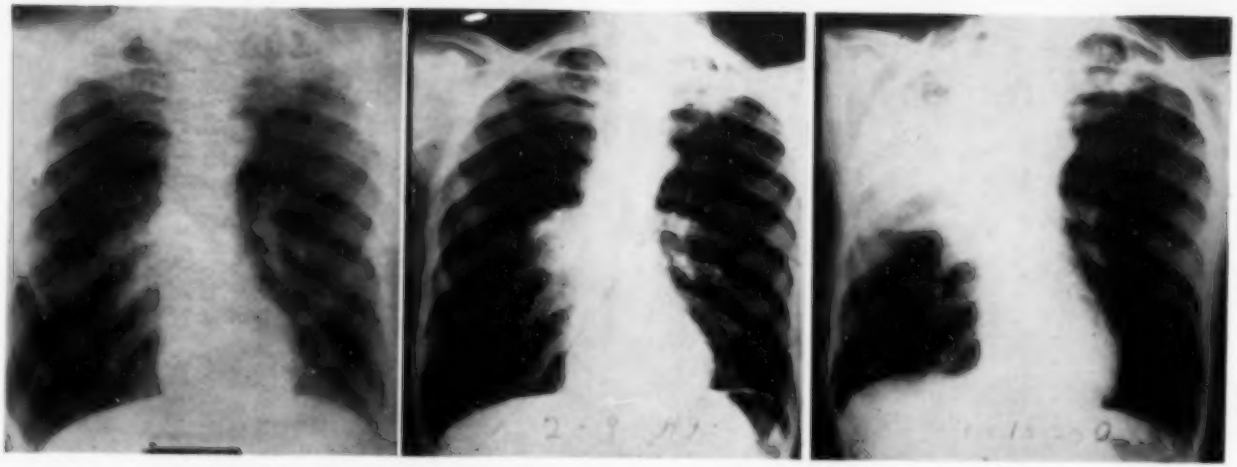

FIGURE 7: F. B., 57 N. Male. Photofluorogram July 26, 1948 read "moderately advanced tuberculosis of indeterminate activity," lesions right mid-lung and left apex. (Obstructive emphysema on right missed.) February 9, 1949, clinic film reviewed by survey physician because of diagnosis of tuberculosis without positive sputum. Patient bronchoscoped but, because only compression was noted, was not explored. January 18, 1950, obvious carcinoma. Explored, inoperable. Repeated positive sputa and biopsy showing squamous cell carcinoma. Died December 3, 1950.

squamous cell carcinoma. Repeated positive sputa grew out on culture. The patient died December 3, 1950, having had both active tuberculosis and bronchogenic carcinoma.

Delay in Hospitalization

The following data are based on 57 patients with a minimal three-year follow-up period. Six men entered the hospital without any delay. All died. Twenty-three per cent were hospitalized within one month and 33 per cent within three months. The mortality experience favored those hospitalized after three months (Table XII).

TABLE XII

RESECTABILITY AND THREE YEAR SURVIVAL ACCORDING TO DELAY IN HOSPITALIZATION

Delay	Number of Cases	Number Resected	Per Cent Resected	Alive Three Years After Initial Abnormal Photofluorogram			
				Total	Per Cent	Resected	Per Cent
None	6	1		1		—	
7 days-1 mo.	7	3		—		—	
1 mo.-3 mo.	6	2		—		—	
Total under 3 mo.	19	6	32	1	5	—	—
3 mo.-6 mo.	5	1		1		1	
6 mo.-12 mo.	13	4		2		2	
12 mo.-24 mo.	9	2		2		—	
24 mo.-36 mo.	7	3		2		1	
36 mo.-48 mo.	2	—		2		—	
48 mo. and over	2	1		2		1	
Total more than 3 mo.	38	11	29	11	29	5	13
Over-all Total	57	17	30	12	21	5	9

Two factors may obscure the true relationship between prompt hospitalization and ultimate fate. The first is the emergency admission of those whose photofluorograms at once suggest neoplasm and who are mostly already beyond salvage. The second is the paradoxical situation in which those whose lesions were inconspicuous have a better prognosis than those whose photofluorograms were recognized promptly as being abnormal[8]. One must consider that some whose lesions were missed no doubt developed serious clinical illness or died without returning to the units so that the "erroneous negatives" in our study are probably underestimated and may be selected on the basis of slow tumor growth.

At any rate, both the poor prognosis of those with obvious tumor and the better prognosis of those whose lesions were inconspicuous are really facets of the same problem: the photofluorographic picture of curable lung cancer has not been delineated. At one end of the scale we rush patients into the hospital only to have them die shortly. At the other end of the scale we ignore for months or years unimpressive x-ray abnormalities and, even then, we salvage some of them.

There is a trend in our series toward increasingly prompt hospitalization. Table XIII reveals that twice as high a percentage was hospitalized within three months among those with less than three years' follow-up as among those with more than three years' follow-up.

TABLE XIII

DELAY IN HOSPITALIZATION ACCORDING TO LENGTH OF FOLLOW-UP

Delay	Follow-up on those with photofluorograms taken 1-1-47 to 8-31-50		Follow-up on those with photofluorograms taken 8-31-50 to 5-31-53	
	Number	Per Cent	Number	Per Cent
Less than 3 mo.	19	33	34	79
3 mo. and over	38	67	9	21
Total	57	100	43	100

More rapid hospitalization may well be due to the increased index of suspicion in interpreting films as "suspect neoplasm." Of the 43 patients with less than three years' follow-up, 28 (65 per cent) were classified "suspect neoplasm" while, of the 57 in the group with a minimal three-year follow-up period, only 21 (37 per cent) had been so classified. As time goes on, erroneous negatives may turn up among the recent group. This would shift the percentages.

Individual components of delay were examined for the whole group of 100 (Table XIV). There were three causes of significant delay—the radiologist, the patient, and the clinician.

With such low survival rates, it is fallacious to attempt to weigh the causes of delay according to their importance. Certainly the longest delays

TABLE XIV

DISTRIBUTION OF COMPONENTS OF DELAY* ACCORDING TO NUMBER OF CASES INVOLVED AND MEDIAN LENGTH OF DELAY IN HOSPITALIZATION

Cause**		Number of Cases		Median Delay in Days	
Radiologist	Erroneous Negative Report	16	24	577	367
	"Suspect" (Inadequate Reading)	5		34	
	Inactive Tuberculosis	3		90	
Administrative Handling of Case		62		5	
Patient Delay in Accepting Recommendation		28		141	
Clinician Delay in Recommending Hospitalization		52		48	
Hospital bed not available at time of application		20		7	

*Based on 91 cases on whom hospitalization was delayed more than seven days.

**Categories not mutually exclusive.

were due to the missing of lesions. The 16 in this category had a median delay of 577 days. Yet five of these are living, again emphasizing the fact that rate of individual tumor growth is important.

Radiological Problems

Radiological errors were of two types — those in which lesions were missed (16 cases) and those in which lesions had not been classified as "suspect neoplasm" when, on retrospective review, they could have been so classified (25 cases). These are frank errors that can and should be rectified.

There is an additional problem that needs recognition. There are film abnormalities that cannot be considered suggestive of tumor despite the most critical review. We must accept the fact that, just as Newell et al[12] have pointed out their failure to find a reliable classification of the roentgenographic appearance or quality of a tuberculous pulmonary lesion, so we are unable to reliably classify the roentgenographic appearance of curable lung cancer by survey techniques. Once we can accept our limitations, we will recognize the wisdom of considering all photofluorographic abnormalities of the lungs in men over 45 as possibly due to lung cancer. Our highest salvage may well lie in the group whose films least suggest cancer.

The other approach is the follow-up of those with symptoms whose photofluorograms reveal no abnormality. Research in this direction is being conducted through the Philadelphia Pulmonary Neoplasm Research Project[13].

Review of Previous Photofluorograms

There were 29 patients who had available previous "negative" photofluorograms. On retrospective review, 13 of these remained "negative" but 16 had lesions present which had been missed.

The numbers are small but the fate of the "erroneous negatives" was somewhat better than that of the true negatives (Table XV). Not only was survival a little better but, for those who died, the median length of life was 19 months longer (30 months) for the erroneous negatives than for the true negatives (11 months).

TABLE XV

RESECTABILITY AND THREE YEAR SURVIVAL ACCORDING TO REVIEW OF EARLIER FILMS*

Review Classification	Number of Cases	Resected*		Alive		Resected and Alive	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
True Negative	13	6	46	3	23	2	15
Erroneous Negative	16	5	31	5	31	3	19
Total	29	11	38	8	28	5	17

*Limited to 29 cases on whom earlier photofluorograms were available.

Discussion

A significant amount of lung cancer is being detected by mass surveys. Is such cancer curable? Five-year survival rates are not yet available on significant numbers, but, from the experience of official Philadelphia survey teams, there seems little reason to believe that five-year survival rates of survey-detected cases will be better than the surgeons' depressing figures of under 10 per cent.

We believe these facts should be faced honestly and that every effort should be made to encourage the development of new techniques for earlier casefinding.

A truer evaluation of the possible role of surveys would be obtained if the following principles were adhered to:

1. When persistent or unusual respiratory symptoms are present, men over 45 should be referred for diagnostic studies rather than for survey films. One postero-anterior roentgenogram is inadequate even if entirely negative and may well cause false reassurance. Except in a small number of peripherally located cancers, films may continue to appear normal until the occurrence of secondary shadows or gross enlargement of the tumor itself.
2. Men over 45 who have no respiratory symptoms should report for photofluorograms every six months. We have had two cases in which patients have been inoperable one year after a negative photofluorogram.
3. Survey films should be more carefully read. Unimpressive lesions may be as significant as dramatic lesions, particularly if due to active tuberculosis or cancer. One of the soundest methods for improving the quality of survey readings is meticulous follow-up and routine review by the survey medical team of original photofluorograms when cases of lung cancer are proved. Lung cancer deaths as well as newly diagnosed cases among hospital admissions should be routinely checked against survey files. Comparison of later films with survey photoflourograms brings to light errors and automatically enhances the index of suspicion in the mind of the physician-reader.
4. Any abnormality in the chest roentgenogram of a man over 45 should be considered as possible cancer. Since resection offers the only hope for cure at present, physicians should hospitalize promptly all men with such lesions unless there are available serial films and/or histories adequate to diagnose non-malignant disease. At present immediate hospitalization is largely limited to men whose roentgenograms suggest neoplasm.
5. Even when active tuberculosis is proved, the possibility of associated cancer should be carefully considered in men over 45. With antimicrobial therapy and present surgical techniques, it is more conservative to resect a tuberculous lesion than to watch a patient who is not responding clinically or who has a shadow atypical for tuberculosis go on to inoperability.

What is the profile of cured survey cancer? There are five resected survivors with a minimal three-year follow-up. Their ages range from 58 to 65; three are white, two Oriental. Three of the five had unimpressive lesions. Four of the five had squamous carcinoma and the fifth had an adenocarcinoma. Four of the five were preclinical in that their symptoms had not been troublesome enough to cause them to seek medical advice. Not one had been hospitalized within three months after his first abnormal photofluorogram. One had not been hospitalized for more than three years.

Apparently, salvage is limited to those with slow-growing tumors. There is a fertile field for investigation of factors related to rate of tumor growth. Age, type of tissue, and hormonal state are some of the factors that may be involved.

Acknowledgment

The authors wish to express their indebtedness to Mrs. Minerva B. Waissman, R.N., for her assistance in the prompt hospitalizing of patients and to Mrs. Alberta Connor for her outstanding work in the preparation of the material used in this study.

Summary

1. The prevalence per 100,000 of proved bronchogenic carcinoma among 142,156 surveyed Philadelphians on whom appropriate basic data were available was: three for females, 37 for group as a whole, 69 for males, and 284 for males over 45.
2. The survivorship of 100 consecutive cases of proved bronchogenic carcinoma detected by photofluorograms taken from January 1, 1947 to May 31, 1953 at two official Philadelphia survey units is presented. Of the 57 patients with a minimal three-year follow-up period, only five (9 per cent) were resected and alive at the end of the three years after their first abnormal photofluorograms.
3. Exploration was carried out in 52 instances but resection was only possible in 30. Immediate hospital mortality was 17 per cent.
4. Detailed survival studies on the 57 patients surveyed prior to August 31, 1950 suggest a more grave prognosis for those younger than 55, those whose photofluorograms obviously suggested neoplasm or tuberculosis, those with respiratory symptoms severe enough to have caused them to seek medical advice, those with bronchoscopic abnormality of any type, those with undifferentiated carcinomas, and those with concomitant active tuberculosis.
5. Paradoxically, the fate of patients hospitalized within three months of their abnormal photofluorograms was worse than that of those with delays of more than three months. Two factors may obscure the true relationship between prompt hospitalization and ultimate fate. The first is the emergency admission of patients whose photofluorograms at once suggested neoplasm and who were mostly already beyond salvage. The second is the better prognosis of those whose film lesions were inconspicuous.
6. Examination of individual components of delay in hospitalization

revealed three causes for significant delay—the radiologist, the patient, and the clinician.

7. Any photofluorographic abnormality in men over 45 should be considered as possibly due to lung cancer. The highest salvage may well lie in the group whose films least suggest malignancy.
8. Of 29 patients on whom earlier "negative" films were available, 13 were still considered negative on review while 16 had lesions which had been missed. The fate of the "erroneous negatives" was better than that of the "true negatives."
9. With present techniques, less than 10 per cent of survey-detected lung cancer appears curable. Suggestions are made for improving the situation currently, but it is recommended that the search continue for new more effective case-finding techniques.

RESUMEN

1. Entre 142,156 habitantes de Filadelfia en los que se investigó la frecuencia del carcinoma bronquiogénico por cada 100.000—de ellos, y en los que obtuvieron datos adecuados, fué: tres entre las mujeres, siendo 37 en el total del grupo; 69 para los hombres y 284 para los hombres de más de 45 años.

2. Se presentan los datos sobre la sobrevida de 100 casos consecutivos de carcinoma bronquiogénico demostrado, descubiertos por fotofluorogramas tomados desde enero 1, 1947 a Mayo 31, 1953 en dos investigaciones oficiales en Filadelfia. De 57 enfermos con un mínimo de seguimiento de tres años, sólo 5 (9 por ciento) fueron resecados y viven al cabo de tres años después de su primer fiuorograma anormal.

3. La exploración quirúrgica fué llevada a cabo en 52 casos, pero las resecciones fueron posibles sólo en 30. La mortalidad hospitalaria inmediata fué de 17 por ciento.

4. Los estudios detallados de la sobrevida de 57 enfermos antes de Agosto de 1950 sugiere un pronóstico más grave los menores de 55 años. También lo es para aquéllos cuyos fotofluorogramas claramente sugirieron neoplasias o tuberculosis, para aquéllos con síntomas respiratorios bastante severos como para obligarlos a buscar consejo del médio, aquéllos con anormalidades broncoscópicas de cualquier forma, los que tenían carcinomas no diferenciados y los que—concomitantemente padecían tuberculosis.

5. Paradógicamente, la suerte de los enfermos hospitalizados—dentro de tres meses a partir de la fotofluorografía anormal, fuépeor que la de aquéllos con dilaciones de más de tres meses.

Dos factores pueden obscurecer la verdadera relación entre lapronta hospitalización y la suerte final. El primero es la admisión urgente de los enfermos cuyos fotofluorogramas inmediatamente surgirieron neoplasias y que ya estaban para entonces más allá de posible—recuperación. El segundo es el mejor pronóstico de aquéllos cuyas—lesiones a la película son poco relevantes.

6. El examen de los componentes individuales del retardo en la hospitalización reveló tres causantes de retardo importante: el radiólogo, el enfermo y el clínico.

7. Toda anormalidad fotofluorográfica en los hombres de más de 45 años debe considerarse como posibilemente debida al cáncer del pulmón. La más alta proporción de salvaciones bien puede encontrarse en el grupo cuyas películas menos sugieren malignidad.

8. De 29 enfermos en los se obtuvieron películas al principio "negativas" 13 fueron considerados aún negativos al revisarse en tanto que 16 tenían lesiones que habían sido inadvertidas. La suerte de los "negativos por error" fué mejor que la de los "verdaderos negativos."

9. Con las técnicas actuales menos del 10 por ciento de los casos de cáncer descubiertos por la encuesta parece curable. Se hacen sugestiones para mejorar la situación presente pero se recomienda—que se sigan buscando técnicas más efectivas para el descubrimiento de los casos.

RESUME

1. D'après une étude portant sur 142.156 personnes de Philadelphie, le taux de cancer bronchique certain fut de:

3 pour 100.000 pour les individus du sexe féminin
37 pour 100.000 pour le groupe dans son ensemble
69 pour 100.000 pour les individus de sexe masculin
284 pour 100.000 pour les individus de sexe masculin, agés de plus de 45 ans.

2. Les auteurs rapportent les résultats de 100 cas de cancer bronchique avéré dépistés consécutivement par radiophotographie du *1*er janvier 1947 au 31 mai 1953, par deux organismes officiels d'examens systématiques de Philadelphie. 57 malades furent suivis pendant une période au moins égale à trois ans. Parmi eux cinq seulement (9%) furent opérés et étaient encore en vie à la fin de la période de trois ans suivant le jour où fut découverte chez eux une anomalie radiologique.

3. Une intervention exploratrice eut lieu dans 52 cas, mais ce n'est que pour 30 malades que l'exérèse put être réalisée. La mortalité post-opératoire immédiate fut de 17%.

4. Sur les 57 malades suivis avant le 31 août 1950, l'étude détaillée des survivants montre que le pronostic est plus sévère pour ceux qui sont âgés de moins de 55 ans, pour ceux dont les radiophotographies évoquent d'une manière évidente une néoplasie ou une tuberculose, pour ceux qui ont eu des symptômes respiratoires suffisamment sérieux pour qu'ils aillent chercher un avis médical, pour ceux porteurs d'une anomalie bronchoscopique d'un type quelconque, pour ceux porteurs de cancers indifférenciés et pour ceux qui ont une tuberculose active surajoutée.

5. Paradoxalement, l'évolution des malades hospitalisés moins de trois mois après la découverte de leurs anomalies radiologiques, fut plus défavorable que celle des malades hospitalisés dans des délais dépassant trois mois. Deux facteurs peuvent masquer le vrai rapport entre une hospitalisation rapide et l'évolution fatale. Le premier, c'est l'urgence de l'admission des malades dont la radiologie évoque immédiatement une néoplasie; ou qui étaient presque déjà en dehors de toute possibilité d'être sauvés. Le deuxième facteur est le meilleur pronostic de ceux dont les lésions radiologiques étaient incertaines.

6. L'étude des facteurs qui, pour chaque malade, retardèrent l'hospitalisation, révéla trois causes dues au radiologiste, au malade et au praticien.

7. Toute anomalie radiologique chez les hommes âgés de plus de 45 ans devrait entrainer une suspiscion de cancer pulmonaire. La proportion la plus élevée de survie appartient sans doute au groupe dont les films sont le moins évocateurs de malignité.

8. Parmi 29 malades, dont les premiers films étaient considérés comme "négatifs," 13 l'étaient encore lorsqu'un nouvel examen eut lieu, tandis que 16 monstraient des lésions d'abord passées inaperçues. L'évolution des "négatifs par erreur" fut meilleure que celle des "vrais négatifs."

9. Avec les procédés actuels, moins de 10% des cancers pulmonaires dépistés à l'examen systématique apparaissent curables. Les auteurs font des suggestions pour améliorer la situation actuelle, mais ils recommandent que des recherches continuent pour découvrir des techniques de dépistage nouvelles et plus efficaces.

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The Early Diagnosis of Primary Lung Cancer

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The most important factor in the diagnosis of carcinoma of the lung is the awareness of its possible presence. An early correct diagnosis is essential for adequate and correct treatment. Diagnostic methods have been perfected to such a degree that one can expect a positive diagnosis in approximately 75-80 per cent of the cases. In the remainder, the diagnosis can only be determined by thoracotomy.

TABLE I
ANATOMICAL DISTRIBUTION OF LESION

Location	Source	Number	Percentage of Total
By side: 4151 total cases	Right Lung	2208	53.2
	Left Lung	1892	45.5
	Bilateral	51	1.2
By lobes: 2145 total cases	Right upper	633	29.5
	Right middle	125	5.8
	Right lower	290	13.5
	R. Main Bronchus	114	5.3
	Total on right:	1162	54.1
	Left upper	557	25.9
	Left lower	340	15.9
	L. Main Bronchus	86	4.0
	Total on left:	983	45.9

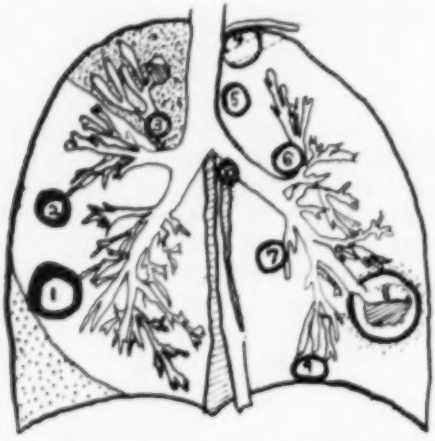
These combined series of cases are adapted from Ochsner, Simons, Gagnon, Gledhill, Aufses, Boyd, and Steele.

Simon,[6] in 1937, reasoned that if carcinoma arises in a random manner the distribution should correspond to the relative weights of the lungs. By calculation, the theoretical distribution in the above case series would be: right lung 2180 and left lung 1971—a close approximation to what was actually found. These calculations were based on the figures given in Gray's *Anatomy*: weight of right lung is 625 grams; weight of left lung is 567 grams. The 51 bilateral growths cannot be taken into the calculation, as they include growths which were probably unilateral initially and the others genuinely bilateral.

In the smaller and more select series where lobar distributions are given, the results are almost precisely the expected figures by calculation based on the relative weights of the lobes. Thus, there is a direct relation between tumor incidence and mass of lung parenchyma.

Winner of 1st Prize 1954 Essay Contest, American College of Chest Physicians.

The Pathogenesis of Symptoms and Signs In Primary Carcinoma of the Lung (adapted from Cecil and Loeb)[8]



1. A tumor near the visceral pleura may produce pleural effusion which may or may not be preceded by "dry" pleurisy. The effusion may be serous, but is characteristically bloody. When actual invasion of the pleura exists, tumor cells may be found in the sediment of the fluid. Dyspnea, a common symptom, may be caused by effusion, but more often is the result of partial bronchial occlusion.

2. Tumors in the parenchyma of the lung may be "silent" for a long period and are discovered only accidentally by routine x-ray examination or by development of a distant metastasis.

3. When a tumor completely occludes a sizable bronchus, the corresponding area of the lung becomes atelectatic. The distal bronchi may become dilated and, depending on the type and virulence of the bacterial flora, pneumonitis or abscess formation results. The physical signs of complete bronchial obstruction must be carefully analyzed, as they closely simulate those of localized pleural effusion. A carcinoma in a large bronchus causes cough by direct irritation of the bronchial wall, but a peripheral growth does not cause cough. This is the commonest symptom, but its value for early diagnosis is reduced since so many men have chronic cough from catarrh or smoking that no great difference is noted when malignant disease supervenes. However, when such individuals develop bronchogenic carcinoma there is usually some alteration in the character of the cough. This is significant.

4. A tumor of the extreme apical region may manifest itself by invasion of the adjacent structures. The superior sulcus syndrome described by Pancoast is: (a) paralysis of the sympathetic trunk resulting in Horner's syndrome, (b) invasion of the first dorsal root of the brachial plexus giving pain referred to the arm and partial paralysis of the ulnar and median nerves, (c) erosion of the ribs demonstrable usually by x-ray examination. The tumor itself may be visualized with difficulty in the x-ray film in early cases. An axillary growth may also cause arm pain by

involvement of the second intercostal nerve, causing pain along the distribution of its intercosto-humeral branch. Intercostal pain may be due to involvement of the chest wall or spine by either direct invasion or blood-borne metastases. Sometimes referred pains may be a striking feature and difficult to explain. A hilar growth may cause severe neuralgic pain in the ear or side of the neck.

5. A primary tumor or metastatic deposit may cause paralysis of the recurrent laryngeal or phrenic nerves on the involved side by direct invasion of the mediastinum and pressure. Hoarseness may be caused by an associated laryngitis with much coughing, but may also result from involvement of the left recurrent laryngeal nerve. It most always occurs on the left side in conjunction with lesions of the left upper lobe. The difference in involvment is due to the lower position of the left recurrent nerve as it passes under the arch of the aorta, as compared to the right recurrent nerve which passes around the right subclavian artery. Recurrent laryngeal nerve paralysis carries a grave prognosis; only 7 per cent or less of cases with this complication can be resected.

Stridor, due to partial occlusion of the trachea or of a main bronchus, occurs chiefly with involvement of the mediastinal nodes. Pressure on, or involvement of, the superior vena cava is also seen in a considerable number of cases, and may be an early or late symptom.

6. A tumor that incompletely obstructs a large bronchus frequently causes a "wheeze" noted by the patient and audible as sibilant râles to the examiner. The wheeze may be localized by the patient or the examiner as unilateral, thus differentiating it from bronchial asthma. Such a partial obstruction may also cause obstructive emphysema or trapping of the air on expiration in the corresponding area of the lung, a phenomenon demonstrable by x-ray films taken in full inspiration and expiration, respectively. Recurring attacks of pneumonitis, diagnosed as bronchitis or bronchopneumonia, punctuate the case history.

7. Ulceration of the bronchial mucous membrane gives rise to blood-streaked sputum or recurrent hemorrhages. This symptom frequently leads to the erroneous diagnosis of pulmonary tuberculosis—a diagnosis that should always be questioned in the absence of positive sputum. An occasional streak of bright red blood which the patient ascribes to too forceful coughing is the usual thing. Uniform pink staining of the sputum daily for some weeks is uncommon, but almost diagnostic when it occurs. Rarely, profuse hemoptysis, or even a fatal one, may occur.

8. Tumors may undergo central necrosis with abscess cavitation and the establishment of bronchial fistula. Empyema may result. The sputum may be foul and abundant, and often blood-streaked. The differentiation between this type of lung abscess and the type uncomplicated by malignancy may become apparent only at operation to establish drainage.

9. Irritation of the central portion of the diaphragmatic pleura by extension of a growth gives pain of typical phrenic nerve distribution.

10. Dysphagia may occur from a growth in a main bronchus involving the esophagus by direct spread. Compression of the esophagus may also be produced by secondary massive involvement of mediastinal nodes, and

those most liable to do this are the ones at the carina and the chain between the pericardium and esophagus.

TABLE II

I. Frequency Distribution of Intial Symptoms in 4771 Collected Cases of Lung Cancer

Symptoms	Per Cent of Listed Cases
Cough	35.6
Chest Pain	20.2
Repeated URI ("Flu; Colds")	10.8
Dyspnea	7.1
Weakness, Fatigue Lassitude	7.0
Hemoptysis	6.7
Pneumonitis	5.4
Extrathoracic Pain (abd., back, shoulder, upper extremity)	4.1
Loss of weight	2.5
Increasing Cough & Expectoration	1.7
Wheezing	1.3
Hoarseness	1.3
Fever	1.0
Dysphagia	0.8
Sundry Other Symptoms: (Congestive failure, headache, chills & fever, neck swelling, paraplegia, cerebral symptoms, metastatic nodules or nodes, clubbing, malaise).	6.0
Routine X-Ray (No Symptoms)	2.1

II. Frequency of All Symptoms in 4117 Collected Cases of Lung Cancer

Symptoms	Per Cent of Listed Cases
Cough	73+
Sputum	54.5
Chest Pain	53.8
Weight Loss	48.5
Hemoptysis	45.0
Dyspnea	40.1
Weakness, Fatigue, Lassitude	35.3
Respiratory Infection	34.1
Substernal Discomfort	33.6
Wheeze	19.8
Extrathoracic Pain (e.g., abd., Pancoast Syndrome)	12.0
Fever	11.5
Anorexia	8.3
Night Sweats	8.0
Hoarseness	7.1
Hypertrophic Osteoarthropathy	7.0
Obstruction of Sup. Vena Cava	5.8
Tightness in Chest	3.3
Dysphagia	1.8
Sundry Other Symptoms: (Malaise, paroxysmal hyperpnea, distant metastases, paraplegia, pleural effusion, jaundice, sore throat, hematuria, palpitations, convulsions)	27.6
No Symptoms	2.7

In addition to a careful recording of the history, an ordinary clinical examination (with particular emphasis on the common areas of metastasis, such as supraclavicular area) evaluating the general condition of the patient is the next step in making a diagnosis. It must be remembered that malignant disease does not of itself produce symptoms merely by virtue of its malignancy, and that the picture of a wasted, cachectic patient is a late event and of no clinical importance except insofar as his misery may be alleviated by medical and nursing care.

The interpretation of symptoms must be considered in terms of the processes mentioned above. Only in this way can it be seen how many different pathological lesions can cause identical symptoms, and from this it is a short step towards accurate differential diagnosis and early treatment. There are no physical signs that are typical of lung cancer, except when the tumor is advanced. Any physical signs which may be elicited depend on the size, site, and complications of the growth. In many instances abnormal signs may be entirely lacking. The only chest sign of special significance is unilateral wheezing.

Additional Aids To Making An Early Diagnosis of Lung Cancer

I. Chest X-ray Inspection

X-ray inspection of the chest using both posterior-anterior and lateral films is the most valuable diagnostic method that we have in investigating a patient who may have an early cancer of the lung. This will show some alteration from the normal in about 97-98 per cent of cases. A good roentgenologist can make a presumptive diagnosis of carcinoma of the lung in about 80-85 per cent of the films. The radiolucency of normal pulmonary tissue provides an ideal background for the detection of the densities produced by solid tumors, and their complications. These facts make carcinoma of the lung the most detectable of all internally situated malignant tumors.

Roentgenographic examination should also include fluoroscopy, and, where necessary, spot films, grid films, and tomography (see below for discussion of this). Fluoroscopy of the chest is valuable to show evidence of obstructive emphysema, a "lighting up" of a segment or lobe on expiration, when a bronchus is partially occluded. It also is the only means of detecting paralysis of one side of the diaphragm when it exhibits paradoxical motion as the patient inhales sharply—which would indicate involvement of the phrenic nerve. Pleural fluid is readily detected and located for aspiration by means of the fluoroscope.

It is obvious that an x-ray diagnosis of cancer of the lung is only presumptive. No time should be lost in establishing a definite diagnosis. Serial roentgenograms to determine change in the size of the lesion are not justifiable. The delay entailed may result in the lesion becoming inoperable by the time it is referred for surgical treatment. The demonstration of a lesion in the lung is an indication for prompt diagnosis and definitive treatment—not procrastination.

One must always keep in mind, in the study of x-ray films, that shadows are being interpreted, and that there is nothing diagnostic about the type of shadow cast by lung cancer. Interpretation of the shadow must be made in correlation with the history, the physical signs, the laboratory tests, and findings at bronchoscopy. Absence of a tumor shadow is insufficient evidence upon which to rule out the existence of a lung tumor when symptoms or signs indicate the possibility of its presence. In about 20 per cent of cases an early carcinoma or other bronchial neoplasm casts no recognizable shadows on the x-ray film or is concealed by shadows of other structures.

Though the discovery of small, non-symptomatic pulmonary lesions by roentgenograms offers the best diagnostic avenue to curative treatment, it is also of great value in those lesions producing symptoms. Again, the absolute diagnosis must, generally, await microscopic examination of tissue. The roentgenographic demonstration of metastatic lesions in bone or soft tissue may aid in demonstrating the extent of the disease and futility of operative intervention in such instances.

It *is* possible to make the diagnosis of lung cancer early, for it has been shown that it has a greater duration from its inception until death than

has hitherto been considered. In a small combined series of inoperable cases, the average minimum duration of life from the onset of the earliest sign was 30.2 months. *Roentgen findings are usually present in the presymptomatic stages of the disease, and are almost invariably present after the onset of symptoms.* The earliest x-ray evidence of the disease has been recorded as long as nine years before the death of the patient, and as long as four and one-half years before the onset of symptoms.

TABLE III
FREQUENCY OF ROENTGEN FINDINGS AND OPERABILITY IN LUNG CANCER

X-Ray Finding	Frequency in Per Cent	Per Cent Operable
Atelectasis (massive or segmental)	62	23.4
Neoplastic Infiltration (central of peripheral)	38	24.8
Hiler Shadow	26	13.5
Cyst, Abscess, or Cavity	6	43.3
Round Tumor	5	66.6
Effusion	3	8.3
Mediastinal Tumor	2	14.3
Patch of Increased Density	0.6	50.0
No Abnormality	1.3	—

These combined series of cases are adapted from Mason, Strang, Steele, Reinhoff, Björk, Linvaag, and Therkelsen and Sørensen.[11]

II. Exfoliative Cytology.

Bronchoscopy and cytologic examination of exfoliated cells should be the next steps in establishing a diagnosis. The histological examination of the sputum or clumps of malignant cells may facilitate the diagnosis when more accurate methods are not available. It is usually not safe to make a diagnosis of malignant disease by looking through the microscope at cells isolated from their surroundings, but an experienced pathologist may often be able to give information, which, taken in association with all the other evidence, may be conclusive. A positive result of the cytological examination of the sputum may serve to supplement the other diagnostic procedures, but it must not decide the diagnosis. A negative result is of no significance.

Any sputum expectorated by the patient should also be carefully examined for tubercle bacilli, predominating pyogenic organisms, and fungi. A positive laboratory report for any of these organisms, should, however, be correlated with the history, physical, and appearance of x-ray films, since any of these conditions may be present in addition to carcinoma.

Several workers have noted that the study of at least three consecutive specimens per case is required for greatest accuracy; if adequate specimens are obtained the number of correct positive reports could be raised to 75 or 80 per cent for all cases, and for the resectable cases it could be raised to 85 per cent. When five or more sputum specimens are submitted,

88-100 per cent of proved cases of lung cancer were diagnosed by cytologic methods. When only one specimen was submitted, or when incomplete sputum studies were offered for examination, only 61-66 per cent of proved cases were diagnosed. The identification of the type of tumor from exfoliated cells is not reliable.

In the opinion of many workers using cytologic methods, this method of diagnosis should be restricted to cases with signs and symptoms of tumor, but without an available positive histologic diagnosis. It is not practical as a screening procedure since too much time and expense are involved. The cytologic diagnosis added to clinical and x-ray evidence in the absence of positive biopsy may be sufficient to sway the balance toward pneumonectomy. Even though certain cell patterns are practically diagnostic, frozen section should be done at thoracotomy when bronchoscopic biopsy is negative, even if the cytologic diagnosis has been positive, in order to reduce error to practically zero.

Specimen for specimen, examination of aspirated secretions for neoplastic cells is more valuable than examination of sputum, but because one can examine many sputum specimens whereas one does relatively few bronchoscopic examinations, the sputum examinations give more correct diagnoses. However, the purpose of this whole procedure is to arrive at an 'early' diagnosis of cancer, and, as shown in Table II, early in the course of the disease there is little or no sputum.

III. Bronchoscopy.

Bronchoscopic examination under local anesthesia is a minor outpatient procedure which should not be omitted. Growths in the main bronchi and their primary divisions may be seen and biopsies taken. The secondary effects in the bronchial tree, such as deformity, compression by extraneous lesions, rigidity, displacement, infiltration of the carina, and lack of mobility of the vocal cords, may be helpful even when the growth itself cannot be seen. Rabin[5] et al concluded that a biopsy specimen of the mucous membrane of the main bronchus within one centimeter of the carina should be taken in all cases of bronchoscopically demonstrable primary carcinoma considered for operation. A positive paracarinal biopsy of mucous membrane that appears normal indicates the presence of submucosal lymphatic spread, and this serves as a contra-indication to any type of pneumonectomy performed with a view to cure.

A negative bronchoscopic examination in no way rules out a bronchogenic lesion, a large number are beyond the bronchoscopic range of vision. It is important to remember that bronchoscopy which is negative at the onset of a long period of observation may give positive findings when repeated later.

A note of warning might be interjected here in regard to taking a biopsy through a normal and intact mucous membrane. There are recorded cases of death in such instances, due to exsaguination following rupture of a hemangioma, non-pulsating aneurysm of the aorta, and aneurysm of the inominate artery. An angiogram, of course, would avoid these catastrophes.

IV. Bronchography and Tomography.

Neither of these procedures is usually necessary for the diagnosis of lung cancer, since bronchoscopy is usually more informative. They are especially valuable for the growth in a bronchus inaccessible to bronchoscopy. Forster et al[2] claim that transversoaxial tomography (cutting transversally the intra-thoracic organs with a vertical axis giving direct knowledge of the degree of fixation of tumor to these organs) is a valuable help in the estimation of the operability of pulmonary cancer. Tomography will also distinguish between an abscess and the cavity of a neoplasm which is breaking down.

V. Angiocardiography.

By means of angiocardiography, a technique has developed for differentiating between unresolved pneumonia (increased or normal vascularity of the involved segment) and bronchial carcinoma (decreased vascularity). Definite criteria have been worked out for assessing the inoperability of bronchial carcinoma by angiocardiography.[9] This is a safe procedure to perform[3]—the mortality being less than 0.5 per cent—the only contraindications being sensitivity to iodine-containing compounds, severe renal disease, and infants with severe cyanotic congenital heart disease.

VI. Cine-densigraphy.

This new method involves the photo-electric registration of very small amplitudes of density fluctuation, i.e., the capillary pulse of the lung. Supposedly, there is no capillary pulse in malignant tumors and a normal capillary pulse in benign tumors.[7]

VII. Needle Biopsy.

The general consensus of opinion in this country is that needle biopsy should not be performed on patients who might have an operable lesion, for fear of further spreading the tumor by implantation of tumor cells in the tisues tranversed by the biopsy needle. When a curative resection is contemplated, one would be loath to accept a negative report from such a procedure, and since direct exploration of the lesion will be done, it would seem to be a superfluous examination that might, in some instances, compromise the patient's chance of cure.

VIII. Thoracentesis.

When pleural fluid is present, it should be aspirated and examined. If the fluid is grossly bloody, the lesion is probably inoperable. The centrifuged sediment of the pleural fluid should be examined for neoplastic cells; if present, the lesion is inoperable. Late in the disease, tumor cells may be found in the pleural fluid in about 50 per cent of cases.

IX. Lymph Node Biopsy.

Any suspicious lymph nodes or subcutaneous nodules of recent origin should be removed and examined microscopically before definitive therapy is instituted. In the absence of palpable supraclavicular nodes, removal of lymph-node-bearing adipose tissue overlying the supraclavicular portion of the scalenus anterior muscle can be done under local anesthesia.

X. Diagnostic Pneumothorax and Thoracoscopy.

Diagnostic pneumothorax is not often necessary and less often helpful. It has a place, however, where a shadow blends with the mediastinum and doubt exists as to whether it is in the mediastinum or lung. If pleural adhesions are not too numerous, the induction of a pneumothorax followed by radiography, or even thoracoscopy, may decide the point.

Thoracoscopy is also an adjunct in the differential diagnosis and the prognosis of intrathoracic lesions. For example, thorascopic examination is of value in determining extension to the pleura. In addition, the possibility of surgical removal can be ascertained in many cases without subjecting the patient to thoracotomy.

XI Exploratory Thoracotomy.

It is probable that the more frequent use by competent surgeons of exploratory thoracotomy in those patients where the diagnosis of lung cancer is suspected, at a stage where it cannot be proved, will lead to greatly improved results of treatment. The majority of writers both here and abroad, feel that exploratory thoracotomy is justified in all cases in which there is suggestive evidence of lung cancer, but in which the diagnosis cannot be established pre-operatively despite thorough studies (this happens in about one-fourth of cases). This is especially true in the silent or relatively asymptomatic lesions. Indeed with the more widespread use of routine examination of the chest by x-ray and fluroscope, and the more frequent detection of asymptomatic lesions by this means, exploratory thoracotomy will be the only means of establishing the diagnosis in a very high proportion of cases.

Exploratory thoracotomy is felt by most surgeons to have the same degree of safety as exploratory laparotomy (and with less discomfort to the patient). To wait to see what develops in a patient who offers suggestive evidence of pulmonary neoplasm is to let the opportunity for cure be forever lost in many instance. Even benign appearing tumors should be explored promptly because many of them are actually malignant; the majority of the others have malignant potentialities, they will eventually produce bronchial occlusion with suppurative complications, and even those most completely benign will (with continued growth) assume a size sufficient to crowd contiguous and vital structures with untimely death of the patient.

XII. Mass Surveys.

Roentgen radiological surveys now bring to light well-defined shadows in the chest when there are no physical signs of symptoms. Some of these are lung cancers, but they may be tuberculomata, fluid-filled cysts, inspissated abscesses, benign bronchial tumor, or secondary malignant deposit from an unknown primary. A breaking down carcinoma may resemble a lung abscess.

Regular semi-annual chest x-ray films of men over 45-50 on a voluntary basis might be of value. However, it remains to be shown whether apparently early lesions in such men will actually be subjected to surgery,

whether the usual delay of 3-18 months before treatment can be reduced, and whether surgery will be effective in curing the disease in a majority of cases. From the practical viewpoint, it is believed that mass chest surveys of the general population for the detection of lung cancer are *not* a useful or effective weapon. The average yield is less than 16 per 100,000 persons x-rayed; the cost is very great; the practical problem of staffing the survey units with competent and interested persons is almost insuperable.

One must remember that from one-third to one-half of primary lesions are hilar in location or otherwise so situated that single posterior-anterior survey films will not reveal them, and also that a considerable number of patients go to survey centers because they already have chest symptoms.

On the credit side stand the findings of Overholt and Woods[4] who examined 7,892 persons in a chest roentgenographic survey: 67 underwent surgical exploration for tumors, and 39 (60 per cent) of the tumors proved to be malignant. Of particular significance is the fact that among the patients in their series in whom carcinomas of the lung were found in the asymptomatic phase by survey roentgenograms and were promptly explored, *all were resectable* with no evidence of lymphatic extension in 70 per cent.

SUMMARY AND CONCLUSIONS

The following table summarizes the value of some of the examinations listed above in the making of a diagnosis of lung cancer:

Procedure	Per Cent of Diagnoses Made
Clinical Exam. and History	60.7
X-Ray	82.5
Bronchoscopy	51.4
Biopsy	45.4
Exfoliative Cytology	69.4
Combination of All Methods	76.5

These figures are based on the combined series of some 31 different workers.

There is almost no chest disease which may not be simulated by lung cancer, and it is essential that the methods of investigation outlined above should be applied with expedition if the diagnosis is to be made in time for treatment to be effective. The diagnosis should be made by those methods which upset the patient least, but where the problem persists, all aids must be brought into use without delay. To spend three months looking for the tubercle bacillus while a carcinoma is spreading and when other methods of investigation will yield a quick answer is negligent, and it is not in a patient's interest to watch a shadow for weeks or months radiologically when a bronchoscopic examination may give an immediate diagnosis.

A thorough search of the literature revealed that over the past 14 years 4,376 of 22,095 cases of lung cancer (reported by some 52 authors) were subjected to resection (19.8 per cent); however, the 1954 resectability

rates are practically double those given in 1940—a tribute to an increasingly alert medical population. Since the average duration of symptoms before treatment is instituted is 8 to 13 months, continued vigilance on the part of the physician is necessary; insistence upon accurate diagnoses of lesions appearing within the lung will bring more and more patients having cancer to the thoracic surgeon at a stage where the lesion can be completely removed.

The operative mortality rates with pneumonectomy for cancer of the lung have now been reduced in most clinics to about 5 to 10 per cent. Surgical techniques have been perfected, and there is no doubt of their potentials, yet the best results that the most experienced thoracic surgeons can accomplish is an overall 5 to 9 per cent five-year salvage. Two-thirds to three-quarters of all patients are inoperable when they are first seen. From one-third to one-half of those who are explored have disease that is too far advanced to permit resection, and well over one-half of the resections that are done are merely palliative. However, series are accumulating that show that the five year survival rate *in resected cases* is 18 to 23 per cent; in those patients given "curative" resections the five year survival rate may be as high as 38 per cent. The increase in salvage is not great, but the indications are clear. The more patients who can be gotten to the thoracic surgeon in time for a *curative* resection, the greater is the hope for a successful attack on lung cancer.

RESUMEN Y CONCLUSIONES

El cuadro siguiente resume el valor de algunos métodos de examen para el diagnóstico del cáncer del pulmón:

Procedimientos	Porcentajes de Diagnosticos hechos
Examen clínico e historia	60.7
Rayos X	82.5
Bronchoscopía	51.4
Biopsia	45.4
Citología exfoliativa	69.4
Combinación de todos los métodos	76.5

Estas cifras están basadas en la combinación de las series de 31 autores diferentes.

Casi no hay enfermedad torácica que no pueda ser simulada por el cáncer del pulmón, y es esencial que los métodos de investigación señalados antes, sean aplicados diligentemente si se pretende hacer un diagnóstico a tiempo para que el tratamiento sea eficaz. El diagnóstico debe hacerse por los métodos que molesten menos al enfermo pero cuando el problema persiste sin resolverse, todos los demás procederes deben ponerse en juego. El pasarse tres meses buscando elbacilo de la tuberculosis mientras que un carcinoma se propaga, cuan do hay otros métodos de investigación que pordrían dar una respuesta inmediata, es dar muestras de negligencia y para bien del enfermo no es de interés el vigilar una mancha por semanas o por meses radiológicamente cuando an examen broncoscópico puede dar la respuesta diagnóstica inmediata.

Un examen completo de la literatura reveló qu en los pasados—14 años 4,376 de 22.095 casos de cáncer del pulmón (relatados por 52 autores) se sujetaron a resección (19.8 por ciento). Sin embargo, la proporción de casos resecables en 1954 es práticamente el doble de la proporción dada en 1940, lo que es un tributo a una población médica más alerta.

Puesto que la duración media de los síntomas antes del tratamien to es de 8 a 13 meses, se requiere una contínua vigilancia por parte del médico. La insistencia sobre diagnóstico exacto de las lesiones que aparecen en el pulmón puede acarrear más y más enfermos de cáncer del pulmón al cirujano de tórax en una etapa en que la lesión puede eliminarse por completo.

La mortalidad operatoria por neumonectomía por cáncer, se ha reducido ahora en la mayoría de las clínicas al 5 a 10 por ciento. Las técnicas quirúrgicas se han perfeccionado y no hay duda respecto de sus posibilidades y sin embargo, los mejores resultados que los cirujanos más experimentados pueden alcanzar es un porcentaje de rescates de 5 a 9.

De dos tercios a tres cuartos de todos los enfermos son inoperables cuando son vistos por primera vez. De un tercio a la mitad delos que son explorados cuirúrgicamente, tienen la enfermedad demasiado avanzada para realizar la resección, y más de la mitad de las resecciones realizadas son sólo paliativas.

Sin embargo, se están acumulando series que demuestran que la sobrevida de 5*años en los caso resecados* es de 18 a 23 por ciento; en los enfermos a los que se hacen resecciones "curativas" el término de sobrevida de 5 años se alcanza en el 38 por ciento; el aumento de los rescates no es muy grande, pero las indicacionesson claras. Mientras más sean los enfermos que lleguen a las manos del cirujano de tórax en tiempo adecuado para realizar resección "curativa," mayor esperanza habrá de un ataque fructuoso sobre el cáncer del pulmón.

RESUME

La table ci-dessous résume la valeur des différents examens qui ont été cités dans l'article, commne capables de faire le diagnostic de cancer du poumons:

Technique	Pourcentage de diagnostics faits
Historie de la maladie et examens cliniques	60.7
Radiologie	82.5
Bronchoscopie	51.4
Biopsie	45.4
Cytologie bronchique	69.4
Combinaison de toutes les méthodes	76.5

(Ces chiffres sont établis en additionnant les statistiques d'environ 31 auteurs différents).

Il n'y a pratiquement aucune affection pulmonaire qui ne peut être simulée par le cancer. Il est indispensable que les méthodes d'investigation qui viennent d'être soulignées soient appliquées rapidement afin que le diagnostic précoce permette un traitement efficace. Il y a intérêt à ce que le

diagnostic puisse être établi grâce aux méthodes qui sont le moins pénibles pour le malade. Toutefois, quand le problème reste sans solution il faut mettre en oeuvre toutes les possibiltés sans attendre. Doit être considéré comme négligent quiconque perd trois mois à la recherche de bacilles de Koch, alors que le cancer s'étend, tandis que d'autres méthodes de recherches auraient pu fournir une réponse rapide; l'intérêt du malade n'est certes pas de surveiller une ombre radiologique pendant des semaines ou des mois lorsque la bronchoscopie pourrait donner un diagnostic immédiat.

Une étude exhaustive de la littérature montre qu'au cours des quatorze dernières années, sur 22.095 cas de Cancers pulmonaires (rapportés par environ 52 auteurs) 4.376 cas, c'est-à-dire 19,8% furent soumis à l'intervention. Cependant la proportion de cas opérables en 1954 est pratiquement le double de celle de 1940. Ceci doit être attribué à l'accroissement de l'attention des médecins dirigée dans ce sens.

Comme en moyenne la maladie a déjà évolué depuis 8 à 13 mois lorsque le traitement est institué, il est nécessaire que le milieu médical continue à se préoccuper de ce problème. En insistant sur la nécessité d'accélérer le diagnostic des affections pulmonaires, on arrivera à amener de plus en plus au chirurgien les malades atteints de cancer pulmonaire, alors que leurs lésions peuvent être extirpées radicalement.

Les chiffres de mortalité opératoire après pneumonectomie pour cancer du poumon se sont réduits actuellement dans la plupart des centres chirurgicaux aux environs de 5 à 10%. Les techniques chirurgicales ont été perfectionnées et personne ne doute de leur valeur. Cependant les meilleurs résultats obtenus par les chirurgiens thoraciques les plus expérimentés n'arrivent qu'à 5 à 9% de succès après 5 ans. Les deux-tiers ou les trois-quarts des malades ne sont plus opérables quand ils sont vus pour la première fois. Parmi ceux qui sont l'objet d'une thoracotomie, le tiers ou la moitié sont atteints d'une affection trop évoluée pour qu'on puisse pratiquer une exérèse et dans l'ensemble, la moitié des exérèses qui sont pratiquées sont simplement palliatives. Toutefois des statistiques de plus en plus nombreuses montrent que dans les cas opérés, la survie atteint 5 ans dans 18 à 23% des cas. Chez les malades pour lesquels l'exérèse a été vraiment curative, la moyenne qui arrivent à 5 ans de survie s'élève à 38% L'augmentation des succès n'est pas considérable, mais les indications sont claires. Plus nombreux seront les malades qui pourront être amenés au chirurgien thoracique à temps pour qu'il pratique une exérèse curative, plus se développera l'espoid d'une action heureuse sur le cancer pulmonaire.

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CURRENT DATA ON CARCINOMA OF THE LUNG

Clemmesen et al recently reported that there is a difference in the mortality rate for different sections of the population in Denmark. This report indicates that there is a delay in onset of the carcinogenic influence of about eight years for provincial towns and about ten years for rural area. The authors discount any carcinogenic influence of atmospheric pollution as far as Denmark is concerned. They have assumed that the carcinogenic influence does not begin earlier than the fifteenth year of age and that it takes at least 20 years from the beginning of the exposure to the carcinogenic effect until the death of the patient. They conclude that an urban area such as Copenhagen began to exert its carcinogenic influence between 1900 and 1910. Clemmesen, J., Nielsen, A., and Jensen, E., "The Increase in Incidence of Carcinoma of the Lung in Denmark, 1930-1950," *Brit. J. Cancer 7:1.*

Phillips analyzes deaths in Canada from lung cancer for the years 1931-1952. In 1931, deaths reported as due to lung cancer represented 2.2 per cent of all cancer deaths. This figure increased 400 per cent to 8.7 per cent in 1952. While the female increase rose from 1.4 per cent to 3.2 per cent, the male increase was from 3.0 per cent to 13.4 per cent. The maximum mortality rates for males and females for the period 1950-1952 occurred at 65-69 years and 70-74 years, respectively. The ratio of male to female deaths from lung cancer has increased from 1.9 to 1 in 1931 to 4.9 to 1 in 1952. Phillips, A. M., "Mortality from Cancer of the Lung in Canada, 1931-1952," *Canad. M.A.J. 1954, 71:242.*

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Kreyberg of Norway reports an increase of 700 per cent in males and over 400 per cent in females in lung cancer from 1930 to 1950. The author points out that there is a real increase in the incidence of lung cancer in males, while the increase in female mortality is a reflection of increased diagnostic efficiency. Kreyberg, L., "The Occurrence of Lung Cancer in Norway," *Brit. J. Cancer 1954, 8:208.*

Lew indicates an increase of approximately 700 per cent in the number of deaths from lung cancer from 1930 to 1953 in the United States. While half of this increase is reflected in the growth and aging of the population of the United States, there is little doubt that, in addition to improved diagnostic methods and extensive case finding, a very definite part of the increase represents a *real* increase. The author further reports that the increase in the death rate has been much more rapid in males than in females. Lew, E. A., "Trends in Respiratory Cancer Mortality," *Statistical Bull., Metropolitan Life Insurance Company 1954, 35:10.*

Favorable Bronchiolar Carcinoma

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Operable bronchiolar carcinoma usually is sufficiently characteristic in clinical manifestation, histological pattern and predicted behavior so that it can be recognized individually, not only for its favorable prognosis, but also as a guide to a logical program of therapy. The fact that bronchiolar carcinoma may be an operable and characteristic entity was brought to our attention when one of us (J. E. D.) reviewed all cases of proved bronchogenic carcinoma seen in the Overholt Thoracic Clinic from July, 1950, to July, 1951. It was found that from 49 cases classified as adenocarcinoma, there were only six in which the tumor was localized at the time of resection. Of these six, five had been classified as papillary adenocarcinoma. More significantly, there were no other papillary cancers in this series. These five lesions had been discovered originally by survey, all were located peripherally and all were of long duration by serial roentgenograms.

For a more comprehensive study, we extended the examination to include all bronchogenic carcinomas which were observed in the Clinic between July, 1948, and July, 1953—a total of 507. These yielded only three additional lesions classified as papillary adenocarcinoma. In reviewing the histological sections on all known adenocarcinomas during this period, however, seven additional cases were found which had a comparable histologic pattern. Most of these had been labeled mucinous adenocarcinoma.

Pathology

Grossly, the lesions were of two general types: The first was a diffuse, irregular, massive involvement of lung parenchyma in a manner resembling pneumonic consolidation. The cut surfaces of this type were yellow-gray, often mucinous, sometimes to a degree suggesting small cysts, but gross necrosis was absent. The other type was nodular in nature, with a single, or several nodules from 1.0 to 5.0 cm. in diameter. Some of the nodules showed central necrosis and occasionally umbilication. The gross resemblance to tuberculosis or to metastatic carcinoma was often striking. Microscopically, the typical appearance was of tall, columnar cells in single or multiple layers arranged in glandular formation and lining small bronchiolar and alveolar spaces. The individual cells resembled those of mucus-secreting respiratory epithelium. Frequently, the individual cells contained large droplets of mucus and, at times, pools and lakes of mucus were present in luminal spaces. Histologically, these typical cells appeared

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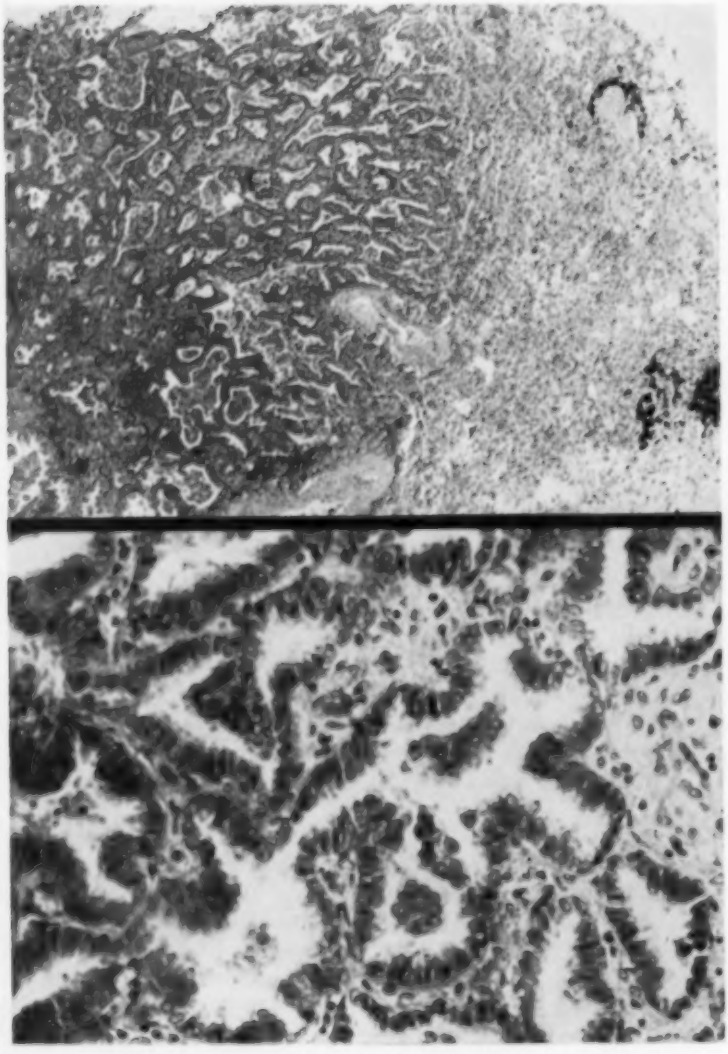

FIGURE 1, *top*: Photomicrograph x50, showing demarcation of bronchial carcinoma from adjacent compressed lung. Although these tumors often appear well circumscribed grossly, there is a lack of microscopic encapsulation and the exact border between tumor and uninvolved lung is often indistinct.

FIGURE 2, *bottom*: Photomicrograph x500, showing a common growth pattern of bronchiolar carcinoma. The cells show uniformity in size and are arranged in a serpentine fashion. Features indicative of anaplasia or of rapid growth, such as cellular pleomorphism, mitoses, are usually lacking.

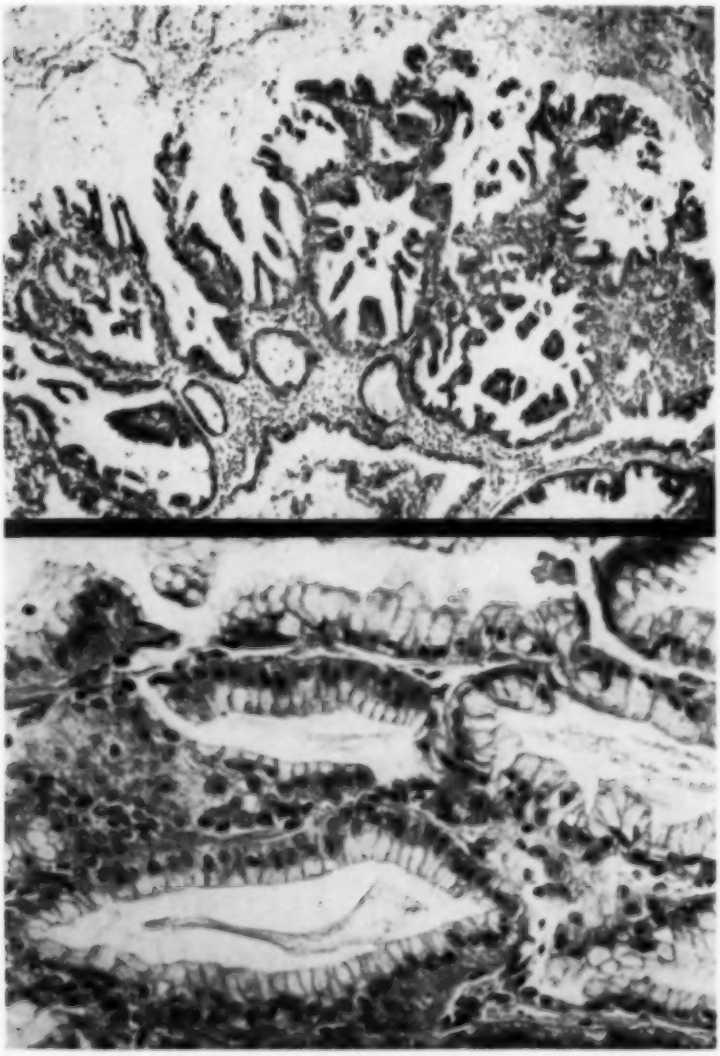

FIGURE 3, *top:* Photomicrograph x150, showing papillary arrangements of tumor cells. Although this pattern of growth is not common, it is sometimes seen in bronchiolar carcinomas, and accounts for the occasional synonym "papillary."

FIGURE 4, *bottom:* Photomicrograph x500, showing a typical mucinous pattern of bronchiolar carcinoma. Not only do individual cells contain large droplets of mucus on their lumen borders, but the luminal spaces also are partially filled with mucus. This case also demonstrates the characteristic lack of undifferentiation and rapid growth.

TABLE I: FAVORABLE BRONCHIOLAR CARCINOMA

July, 1948 — December, 1953

No.	Case	Age	Date of Op.	Duration of X-ray Evidence	X-Ray Findings Early	X-Ray Findings Late	Location	Mediastinal and Hilar Nodes	Extent of Resection	Op. Sur.	Op. Comp.	Post-Op. Hospital Days	Last Follow-up	Remarks
1.	E. B.	64	5/12/48	8 yrs.	"Coin" Lesion	6 cm. Periph Mass	RLL	NEG.	Lobec.	Yes	None	13	.....	Died 2 yrs. 8 mos. Post-op. Developed recurrence 11/49. Pn. completed 11/30/49. Met. to 1 node present at this time.
2.	M.K.	54	12/9/48	7 mos.	"Coin" Lesion	3 cm. Periph Mass	LUL	NEG.	Pn.	Yes	None	12	.....	Died 2 yrs. Post-op. Wide spread met.
3.	S. B.	54	9/20/49	2 yrs.	"Coin" Lesion	3 cm. Periph Mass	RLL	NEG.	Pn.	Yes	None	11	1/9/54	Alive and well 4 yrs. 4 mos. Post-op.
4.	H. C.	66	3/2/50	3 yrs.	"Coin" Lesion	2 cm. Periph Mass	LUL	NEG.	Lobec.	Yes	None	15	4/23/54	Alive and well 4 yrs. 1 mo. Post-op.
5.	H. F.	49	9/13/50	2 mos.	.....	4 cm. Periph Mass	LLL	NEG.	Lobec.	Yes	None	17	5/25/54	Alive and well 3 yrs. 8 mos. Post-op.
6.	R. A.	63	9/25/50	14 mos.	"Coin" Lesion	5 cm. Periph Mass	LLL	NEG.	Pn.	Yes	None	13	5/21/54	Alive and well 3 yrs. 8 mos. Post-op.
7.	E. M.	60	10/22/51	12 mos.	"Coin" Lesion	13 cm. Periph Mass	LLL	NEG.	Lobec.	Yes	None	9	2/12/54	Alive and well 2 yrs. 4 mos. Post-op.

8.	J. S.	49	12/20/51	2 yrs.	"Coin" Lesion	3 cm. Periph Mass	RLL	NEG.	Lobec.	Yes	None	12	4/22/54	Alive and with recurrence 28 mos. Post-op. Developed homolateral diffuse met. 22 mos. Post-op.
9.	T. M.	46	1/22/52	1 mo.	.....	4 cm. Periph Mass	LUL	NEG.	Lobec.	Yes	None	14	12/28/53	Alive and well 23 mos. Post-op.
10.	M. B.	60	1/31/52	1 mo.	.....	6 cm. Periph Mass	LUL	NEG.	Lobec.	Yes	None	12	5/14/54	Alive and well 28 mos. Post-op.
11.	F. C.	55	4/22/52	1 mo.	"Coin" Lesion	"Coin" Periph Lesion	RUL	NEG.	Pn.	Yes	None	39	2/15/54	Post-op hospitalization prolonged by Radio Active Gold. Alive and well 22 mos. Post-op.
12.	C. B.	67	10/11/52	3 wks.	.....	"Coin" Periph Lesion	LUL	NEG.	Lobec.	Yes	None	17	5/29/54	Alive and well 19 mos. Post-op.
13.	M.G.	46	11/22/52	3 mos.	.....	3 cm. Periph Mass	RML	NEG.	Lobec.	Yes	None	12	2/24/54	Alive and well 15 mos. Post-op.
14.	H. K.	51	4/13/53	1 mo.	.....	Periph "Coin" Lesion	Apex RUL	NEG.	Lobec.	Yes	None	16	.....	Died 7 mos. Post-op. Brain met.
15.	M. S.	55	12/1/53	2 mos.	.....	Diffuse Retro-Cardiac Mass	LLL	NEG.	Lobec.	Yes	None	10	6/2/54	Alive and well 6 mos. Post-op.

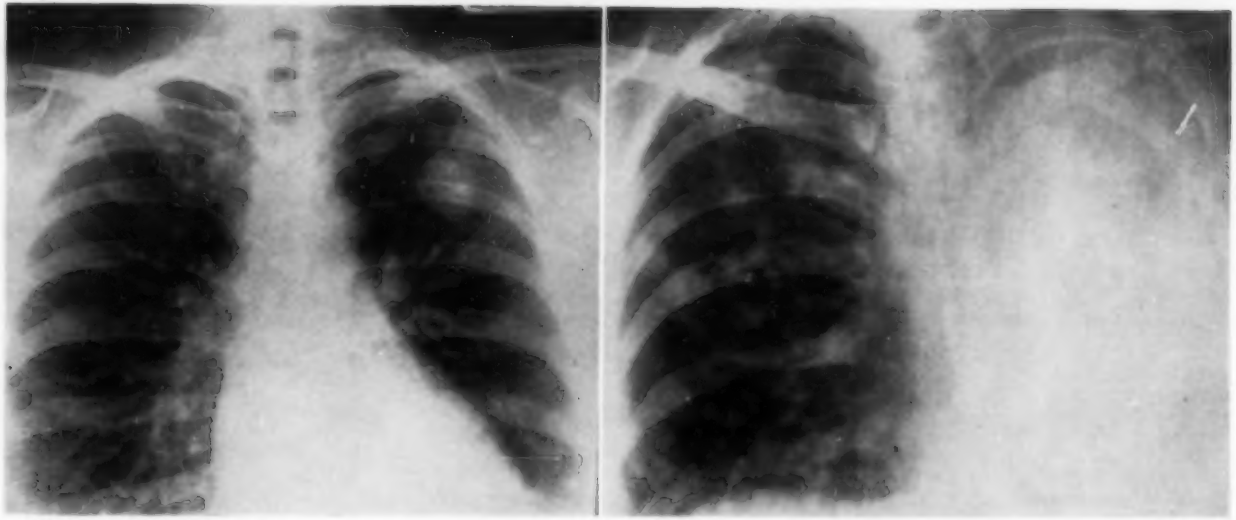

FIGURE 5A

FIGURE 5B

Figure 5A: Case 2 (M. K.). At age 54, this asymptomatic woman had a survey roentgenogram taken which revealed an abnormality in the left lung. Four months later, although the lesion was unchanged in appearance, the left lung was resected. The tumor was bronchiolar carcinoma. Following surgery, the patient remained asymptomatic for 13 months when she developed a persistent cough and began to lose weight.—*Figure 5B:* A roentgenogram disclosed metastatic nodules in the right lung. The patient expired two years following operation.

rather dormant and were quite uniform in nature. In some of the cases, however, there was considerable divergence, at least focally, from this typical cell type so that cells were present which contained little or no mucus, which were more bizarre in structure and which appeared more actively growing, often with mitoses. The stroma was usually scanty; in numerous foci, the cells were arranged about stromal stalks, giving the lesions a "papillary" pattern. The tumors were ill-defined from the adjacent lung tissue and, not infrequently, small clusters of tumor cells were found in the immediately adjacent lung parenchyma. In addition, there was usually an adjacent chronic pneumonitis, similar to that seen in many cases of more usual bronchogenic carcinoma. In only one case did there seem to be involvement of a lymph node by tumor and, in this instance, the node was so completely involved that it could not be identified as such with certainty. Blood-vessel invasion was never found.

The gross and microscopic pathologic appearance of these cases is that of bronchiolar carcinoma, a tumor variously classified under such headings as alveolar cell carcinoma, adenomatosis, papillary adenocarcinoma and mucinous carcinoma (Liebow). They are considered to be carcinomas of a low order of malignancy and, therefore, slow to metastasize, although local parenchymal growth, often becoming bilateral, may be extensive. The 15 cases of this series, since they represent surgical resections, probably also represent relatively early stages of bronchiolar carcinoma and support the contention (Smith, et al) that these tumors are treatable by resection if seen early in their course and that rather than being of multicentric origin, the tumors are monocentric, but have eventual disseminated intrapulmonary metastases. Pathologically, the resemblance of these lesions to either tuberculosis or metastatic tumor may be striking. In particular, lung metastases from mucinous tumors of the gastro-intestinal tract and ovary may be quite similar, both grossly and microscopically.

Clinical Comment

It is unnecessary to report detailed clinical observations in regard to all aspects of this group (See Table I). These patients were between 46 and 67 years of age. Eight were females and seven were males. Symptoms were relatively few and not distinctive. Nine were asymptomatic and, of those with symptoms, cough and occasional hemoptysis were noted. Of significance regarding diagnosis, bronchoscopic findings were negative in each instance and Papanicolaou studies were not of particular value. The diagnosis in each instance was made upon the basis of examination of the extirpated lobe or lung.

Thirteen of the 15 cases were first diagnosed on routine survey films. Eight were classified as "coin lesions" early in the clinical course. Perhaps the most striking feature relative to x-ray findings was the long duration of the lesion by x-ray, plus the paradox of finding all lymph nodes free of invasion at the time of exploration. In one-fifth of the cases, the lesions cast x-ray shadows which were followed for from two to three years be-

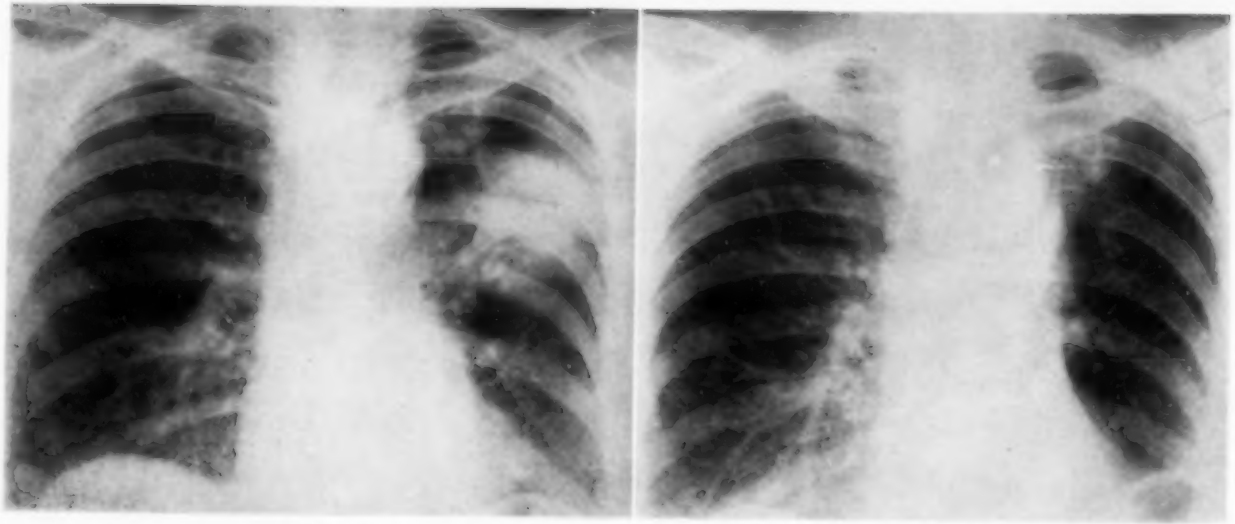

FIGURE 6A

FIGURE 6B

Figure 6A: Case 12 (C. B.). At age 67, this asymptomatic woman had a survey roentgenogram which revealed an abnormality in the left lung.—*Figure 6B:* One month later, the left upper lobe was resected. The tumor was bronchiolar carcinoma. Since surgery, she has remained asymptomatic. At present, no metastases or recurrence can be demonstrated.

fore ultimately coming to surgery. In one instance, the shadow had been present for eight years and, in spite of this long duration, no gross metastases were evident at surgery. In most cases, at the beginning, the family physician or referring doctor considered the small shadow as being innocuous. Only when symptoms occurred or progressive enlargement was evident on subsquent roentgenological examination did the suspicion of carcinoma arise.

Outcome

Follow-up information has been definitely encouraging. Twelve of the 15 cases are now living, and 11 are well, with no evidence of recurrence. Three died after seven months, two years, and the third after three years following operation. One is living with recurrence. Two developed ipsolateral metastatic deposits after lobectomy and are outlined briefly.

Case 1: E. B., age 64, male, with history of a gradually enlarging silent shadow discovered at first by survey in 1940. He had right lower and middle lobectomy in May, 1948. The lesion was large then, but was limited to the lower lobe. All lymph nodes were negative. Frozen section revealed adenocarcinoma and was then thought to be a secondary lesion, probably from a primary in the gastrointestinal tract. A limited resection was elected. Eighteen months later, there was x-ray evidence of recurrence in the right upper lobe. Consequently, pneumonectomy was completed in November, 1949. At the latter operation, one lymph node contained metastases. This patient lived until January, 1951, at which time he died of an unknown cause.

Case 8: J. S., age 49, male, had a positive survey film in 1949. There was gradual enlargement of the shadow subsequently. In December, 1951, upon exploration, a small, discrete mass was found well within the lower lobe. All hilar and mediastinal nodes were negative. Frozen section of a total biopsy obtained by lobectomy raised serious question of a metastatic process rather than a primary lesion. We elected to conclude the procedure with the limited resection and mediastinal node removal. In August, 1953, there developed x-ray evidence of recurrence. Exploration revealed widespread ipsolateral metastases and mediastinal involvement. This patient is now living with disease.

Our experience with all types of pulmonary cancer has been similar to others in that if recurrence takes place it will usually become manifest in the first two years after resection. Seven of these 15 patients with bronchiolar carcinoma have been found to be free of metastases from two years to over four years since the time of resection. Of course, this may be due to the fact that bronchiolar carcinoma is so low grade, recurrences have not had a chance to become manifest. Certainly a longer follow-up period will be necessary for a definitive evaluation.

SUMMARY AND CONCLUSIONS

Fifteen cases of operable bronchiolar carcinoma are herein presented. While it is true that many cases are clinically inoperable when the pulmonary difficulty is first investigated, those patients who do come to thoracotomy, without any gross evidence of extension, either clinically or surgically, probably have a localized lesion. Because of this predictability of the lesion, 11 of these cases were treated by lobectomy. Eight of these are living now, without evidence of disease. For them, the limited resection seem to have been sufficient; and from the point of view of pulmonary function, they will benefit. One of the lobectomy cases was dead in seven months of cerebral metastasis. The two who developed ipso-

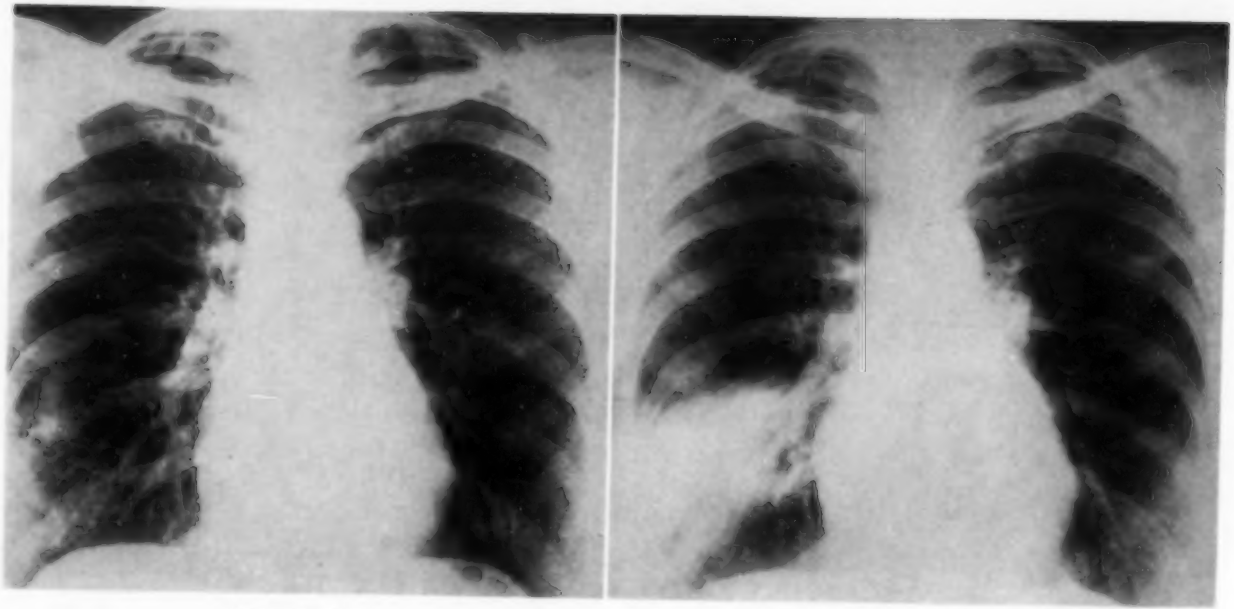

FIGURE 7A

FIGURE 7B

Figure 7A: Case 7 (E. M.). At age 60, this woman was hospitalized for a kidney complaint. The admission film of the chest showed an abnormality in the right lung. She had no pulmonary symptom.—*Figure 7B:* She was watched roentgenographically for 11 months during which time the abnormality became larger. She developed wheeze and productive cough. At that time, right lower lobectomy was performed, and the tumor was found to be bronchiolar carcinoma. For the 32 months since surgery, she has remained completely asymptomatic and without evidence of recurrence or metastases.

lateral disease were under pre-operative observation longer than any of the others—eight and two years respectively.

From experience gained to date with this type of lesion, for localized tumors promptly treated, we believe a conservative type of resection will yield as good results as total pneumonectomy.

RESUMEN

Se presentan aquí 15 casos de carcinoma bronquiolar operable.

Se bien es cierto que muchos casos son clínicamente inoperables cuando la dificultad pulmonar es primeramente investigada, los enfermos que llegan a la toracotomía sin una gruesa evidencia de extensión ya sea clínicamente o quirúrgicamente, tienen probablemente, una lesión localizada. Por esta posibilidad de predecir la lesion de estos casos se han tratado por lobectomía. Ocho viven aún sin evidencia de enfermedad. Para ellos la resección limitada parece ser suficiente; y desde el punto de vista de la función pulmonar se beneficiarán. Uno de los casos de lobectomía murió a los siete meses de metástasis cerebrales. Los dos que desarrollaron enfermedad homolateral estuvieron más tiempo en observación preoperatoria que cualquiera de los demás. (Ocho y dos años respectivamente).

De acuerdo con la experiencia obtenida con esta forma de lesión para los tumores localizados prontamente tratados, creemos que una resección conservadora rendirá tan buenos resultados como la neumonectomía.

RESUME

Les auteurs rapportent 15 cas de cancer bronchiolaire opérable. On sait que bien souvent, les malades sont déjà inopérables quand on constate les premières manifestations pulmonaires. Les malades dont il s'agit ici ont été l'objet d'une thoracotomie, alors qu'il n'y avait pas de signes absolument évidents d'extension tant à l'examen clinique qu'au cours des constatations opératoires, et qu'il était vraisemblable que leurs lésions étaient encore localisées. Cette notion a permis de traiter onze de ces malades par lobectomie. Huit d'entre eux sont actuellement vivants, sans aucun signe pathologique. L'exérèse limitée semble avoir été suffisante pour eux, et ils en tireront le plus grand bénéfice au point de vue de la fonction pulmonaire. L'un des cas opérés par lobectomie mourut au bout de sept mois d'une métastase cérébrale. Les deux malades chez qui l'affection se dévelopa dans le reste du poumon opéré, n'avaient été opérés qu'après une phase d'étude pré-opératoire beaucoup plus longue que celle des autres cas. L'expérience acquise par l'étude de ce type de lésion a amené les auteurs à penser que, pour les tumeurs traitées précocément, une exérèse limitée offre les mêmes bons résultats qu'une pneumonectomie totale.

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Primary Pulmonary Carcinoma

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This paper on primary pulmonary carcinoma is presented with stress on:

1. The Role of Chronic Irritants to the Bronchial Mucosa in Primary Pulmonary Carcinoma.
2. The Relation of Increased Span of Life to Increased Incidence of Primary Pulmonary Carcinoma.
3. The Importance of Auscultation in Early Diagnosis of Primary Pulmonary Carcinoma.

There has been much attention brought recently to the frequent occurrence of primary pulmonary carcinoma. In 1912, Adler[1] was able to collect 374 reported cases from the available literature. In 1912 the disease was rare, and then began slowly to increase. One factor responsible for this was the increase in better methods of diagnosis. Fluoroscopy and x-ray films became available, along with bronchoscopy. Yet in spite of improved methods, carcinoma kept increasing by leaps and bounds.

There are other factors to be considered. The span of life during the period of Sir William Osler was shorter than it is today. Carcinoma is increasing as the span of life lengthens.

Primary carcinoma was rarely reported by the clinician and pathologist in 1914. Between 1930 and 1940, the medical profession began to believe there was a very apparent increase in primary pulmonary carcinoma, and began looking for probable causes. Usually where there is no definite opinion there is much literature. Griffini,[2] Baraban,[3] Miller[4] and others had noted that transitional changes can occur in the bronchial epithelium in the bronchus in tuberculosis and infectious diseases. It is because of the power of such transitional changes in the bronchial epithelium that thoughts were naturally turned to it as one of the possible sources of the origin of primary pulmonary carcinoma. Fried[5] stated "that there is evidence that when the disease is found in the lungs it results from a pathologic (excessive) regeneration following chronic inflammation of the bronchial tree." Most of his conclusions are based on the fact that the basal cells have the power of restitution of the bronchial epithelium and also due to the transitional changes noted in the bronchial epithelium in infectious pulmonary diseases. Fried stimulated Ornstein and Epstein[6] to note what happened to the cases of pulmonary tuberculosis admitted to Sea View between 1932 and 1940. They found only 1.3 per cent of pulmonary carcinoma. Tuttle and Womack[7] noted no such occurrence in bronchiectasis.

The causes listed in Table I, following, were compiled by Ornstein from a book published by Simons[8] in 1937, and as stated before, when there is no definite knowledge, there appears to be many causes.

Presented at the Semi-Annual Meeting, Board of Regent, American College of Chest Physicians, Miami Beach, Florida, November 29-30, 1954.

TABLE I
ETIOLOGY OF PRIMARY CARCINOMA OF THE LUNG
64 out of 940 (Simons)

1. Heredity	1. Trauma
2. Chronic Irritation	2. Schneeberg Mine Cancer
a. Chemical	3. Pulmonary Tuberculosis
b. Mechanical	4. Influenza
c. Bacterial	5. Pneumonoconiosis
d. Radioactivity	6. Chronic Lung Disease
e. Thermal	7. Roentgen Rays
	8. Dust Inhalation
	9. Inhalation of Tar Particles
	10. War Gases
	11. Industrial and Occupational Hazards
	12. Tobacco Smoke

Ornstein and Epstein found 26 carcinomas in 2,000 cases which is 1.3 per cent.

An attempt to base the cause of pulmonary primary carcinoma on chronic irritation of the bronchial epithelium has had no definite clinical or pathological support.

Thoracic surgeons continually complain that primary carcinoma is diagnosed too late. How can an early diagnosis be made? Let us consider the pathology of primary carcinoma of the lung. Everybody assumes that all cases arise from the mucous membrane of the bronchi. Therefore the bronchus where the pathology originates will determine both the symptomatology and the roentgenological appearance. It is logical to assume that if a growth arises in the trachea or main stem bronchi, time must elapse before it increases sufficiently to partly or completely obstruct the lumen of the trachea or stem bronchus. On the other hand, less time elapses if the disease arises from the bronchi to the lobes or the segments of the lobe. Therefore, a great deal of time may elapse before anything happens when the main bronchus is involved, and in a short period of time a segment of a lobe can become atelectatic if the tumor should obstruct the smaller bronchus leading to it.

Therefore the first factor to have in mind is the "stethoscope" which unfortunately so many physicians are using so little. The intensity of breathing in each lobe is determined. When a lobe or a segment of the lobe has diminished intensity, suspicion of a carcinoma should at once be aroused (See Fig. 1).

There are many factors that may cause diminished intensity. These factors should be ruled out. At this time it must be said that a tumor may cause a whole lung to become atelectatic because of obstruction to the main bronchus (Figs. 2 and 3). In some cases, the obstruction to the bronchus clears sufficiently in a few days for the lobe to aerate, and the subsequent x-ray film of the lung shows no atelectasis (See Figs. 4 and 5). If the primary tumor is in a bronchus and bleeding or surrounding infection has obstructed the bronchus with a resultant atelectasis of the lung or lobe, in a few days, the blood or infection has been absorbed and

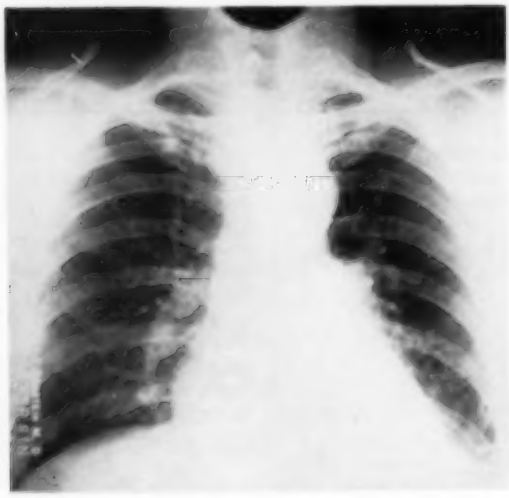

FIGURE 1: Copy of an x-ray film taken 6-3-46 of a man who had some findings in the left lower lobe that suggested change in intensity of posterior segment of the left lower lobe. Bronchoscopy was done and in the left lower lobe an adenocarcinoma was found. Pneumonectomy was done and unfortunately the patient died in a month, yet his initial x-ray film showed little.

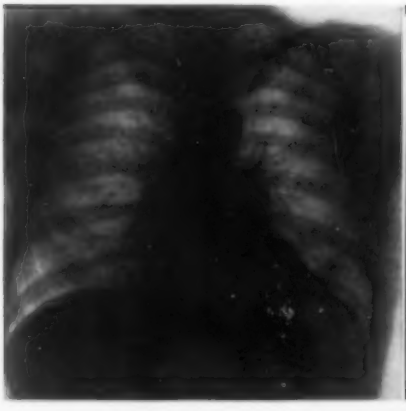

FIGURE 2

FIGURE 3

Figure 2: A print of an x-ray film of a white male, 48 years old. He had been ill for six months with his chief complaint as cough and hemoptysis. He had had one or two bouts of temperature. The x-ray film was taken on 4-18-32. In the left lower lobe there was some infiltrative process which was interpreted as probably that of a bronchectasis with associated inflammatory changes. Patient was bronchoscoped and an adenocarcinoma was found in the left main bronchus.—*Figure 3:* This x-ray film was taken 28 days later. The left lung is almost completely atelectatic. The patient was bronchoscoped at this time. A bronchial carcinoma was found in the main bronchus which grew towards and blocked the bronchus to the left lower lobe. This happens frequently, bronchial carcinoma taking origin in the major bronchus and first blocking the bronchus to the lobe and later blocking the bronchus to the whole lung.

sufficient air passes the obstruction and the lobe becomes aerated again. Auscultation should disclose whether the intensity of the breath sounds is normal or decreased, and the above changes noted.

Carcinoma arising from the trachea and main bronchi may span a long period of time. There may be so little obstruction that changes may be slight enough not to be recognizable. There may be no symptom referrable to the broncho-pulmonary tract. Some symptoms may occur. Degenerative changes may occur. These degenerative changes may provoke bleeding. The sudden appearance of hemoptysis may be the first sign that centers attention to the possibility of primary bronchial carcinoma. There may be no cough or expectoration. Pain may be present, however. The x-ray films may reveal no changes.

If the bloody expectoration has been saved, a Papanicolaou test should be done for malignant cells. Such single hemoptysis should be followed by an exploratory bronchoscopy.

Ornstein and Epstein[6] have discussed thoroughly the symptoms and findings encountered in various phases of obstruction of the bronchi leading to lung or lobes. In their summary they outline the physical and x-ray findings in carcinoma in the bronchus causing little, partial and full obstruction. The authors believe they should again include a chart in this paper.

A. CARCINOMA IN THE BRONCHUS CAUSING LITTLE OBSTRUCTION

Symptoms	Physical Findings	X-ray Findings
1. Cough	1. Usually no abnormal findings.	1. No changes
2. Pain	2. Diminished intensity of breath sounds.	
3. Hemoptysis		
4. No symptoms of toxemia.		

B. CARCINOMA IN THE BRONCHUS PRODUCING PARTIAL OBSTRUCTION

Symptoms	Physical Findings	X-ray Findings
1. Cough	1. Percussion—Dull note over the lung involved. Hyper resonance over the normal lung tissue involved, and exaggerated breath sounds over the normal lung.	1. Involved side smaller on deep inspiration. Shift of the mediastinum to the involved side on inspiration and away on expiration.
2. Pain	2. Diminished intensity of sound over the lung tissue involved and exaggerated breath sounds over the normal lung.	
3. Hemoptysis	3. Sibilant and sonorous rales over the lung drained by the bronchus involved.	
4. Expectoration a. Muco-purulent	4. Shift of the mediastinum (if not fixed) to the side involved on deep inspiration, and away to the opposite lung on deep expiration	
5. Dyspnoea on exertion		
6. Wheezing sensations over the lung involved.		
7. Usually no symptoms of toxemia.		

C. CARCINOMA OBSTRUCTING THE BRONCHUS

Symptoms	Physical Findings	X-ray Findings
1. Cough	1. Percussion—Flat note over the atelectatic lung tissue.	1. Evidence of atelectasis.
2. Expectoration	2. Absence of breath sounds over the atelectatic tissue.	
3. Hemoptysis	3. Vicarious emphysema over the lung tissue not involved.	
4. Pain	4. Clubbing of fingers.	
5. Symptoms of toxemia		
a. Fever		
b. Rapid pulse		
c. Loss of weight		
d. Anorexia		
6. Cachexia		
7. Dyspnea		

We initiated a routine procedure in our office: similar to our procedure of examining every sputum for tuberculosis, we now examine the sputum of every patient past the age of 40 for malignant cells by means of a Papaniculaou test. A negative test for malignancy cannot be interpreted as evidence of no primary carcinoma, but when the test is positive there

FIGURE 4

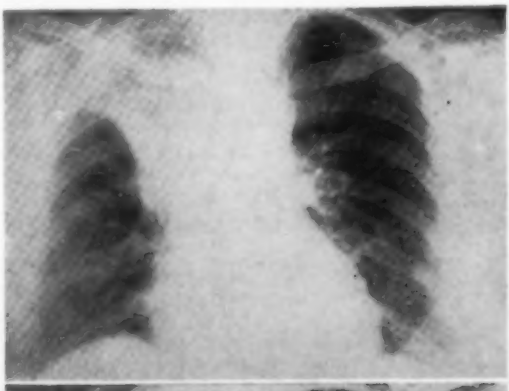

FIGURE 5

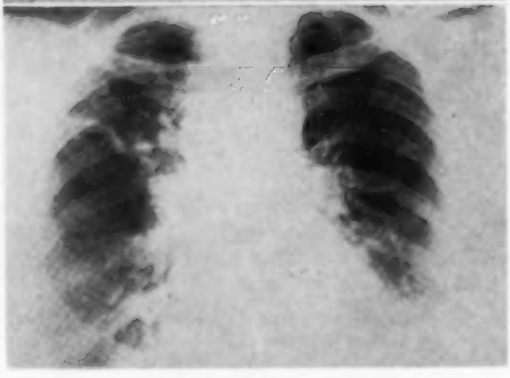

Figure 4: A print of an x-ray film of a white woman of 56 years with an undifferentiated bronchial carcinoma blocking the right upper lobe bronchus and causing an atelectasis of the right upper lobe.—*Figure 5:* A print of the x-ray film of the lungs of the patient described in Fig. 4. X-ray film was taken seven days later. In the interim, bronchoscopic examination revealed a carcinoma blocking the right upper bronchus. A part of the tumor was removed for biopsy and in doing so the bronchus again became patent and the atelectatic lobe had re-expanded. The biopsy revealed an undifferentiated carcinoma.

is no doubt of carcinoma. If the test is reported negative, bronchoscopy should be done, if there is suspicion of a primary carcinoma.

Discussion

The important discussion should be centered on a subject that dates back to 1875 when Griffini[2] presented a paper entitled "Contribuzione alla patologia generale dell tessuto epitelico cilindrico." In 1890 Baraban[3] wrote an article entitled "L'Epithelium de la trachee et des bronches chez un supplicie." There was a question as to the relationship to changes in tracheal or bronchial epithelium due to irritants. Such observations were reported by others and on this thesis Fried[5] wrote a book in 1932 and Simons[8] in 1937 had a list of causes of pulmonary carcinoma due to various irritants. Others have noted changes in structure where the bronchi were irritated but the changes had never been proved to be changes that led to carcinoma, but metaplasia due to hypertrophy of squamous cells. Since it had been suspected since 1875, and again in various ensuing periods, that irritants may lead to changes in the bronchi, it is not strange to hear such a commotion now being made about cigarette smoking. The authors are not impressed. They remember "Buerger's Disease," (thromboangiitis obliterans, where the tibial and dorsal pedis arteries could hardly be palpated) chiefly occurring in a group of Polish Jews that were heavy cigarette smokers. The disease usually was brought to light in the fifth decade. Though in the carcinoma age group, these heavy smokers had little primary carcinoma of the lungs, although the disease and findings are recorded in any standard textbook of pathology. Could you not associate smoking with any adult disease? Cigarettes are so frequently used that you could have a "yes" answer in any adult disease. It reminds us of the relationship of tuberculosis and pregnancy. Tuberculosis of the lungs once occurred chiefly in young adults. The females that married would become pregnant. When the pulmonary tuberculosis was discovered, the pregnancy was associated with the occurrence of the disease, but we now know that it had probably preceded the occurrence of pregnancy.

Regarding irritants to the bronchial epithelium, we have been unsuccessful since 1875 in proving such an association with pulmonary carcinoma. It may be a factor, but until we have sufficient proof, let us not be too sure about the possibility.

The authors believe there is a great increase in the occurrence of primary carcinoma of the lungs since 1914, but there has been a great increase in the span of life since then and as this span lengthens, primary carcinoma will continue to increase. In 1940, we thought there was a considerable increase but since then we find the disease still increasing by leaps and bounds. The span of life has also increased and that may be the answer.

Early diagnosis of primary pulmonary carcinoma is difficult. Perhaps if we do diagnose the disease early, our surgical results may be better. The disease may not have a chance to metastasize to other organs. This frequently happens, and although the thoracic surgeon has done his job thoroughly, the patient does not recover from the metastases to other organs. Early diagnosis of tumors in the trachea and bronchi is difficult

because these tumors may have been embedded for a long time before suspicion of their presence occurs, and they have had a good opportunity to metastasize. Therefore early diagnosis should be stressed. Remember, more can be discovered with the stethescope; x-ray usually is too late. Hemoptysis should be a good lead if there is no accounting for the bleeding. Hemoptysis is usually associated with pulmonary tuberculosis, bronchiectasis and a few other diseases. If you cannot associate hemoptysis with a disease that could be reponsible, a bronchoscopist should look into the trachea and large bronchi. The tumor might be seen or washings may reveal it. Do not rely totally on x-ray changes. In our opinion, more can be learned by auscultation and symptoms.

SUMMARY

1. The best method of early diagnosis of primary carcinoma of the lung is by auscultation (see text).

2. The question of primary carcinoma of the lung occurring due to irritation of bronchial mucous membrane dates back to 1875, and has been frequently revised since.

3. The span of life since 1914 has been increased, and primary carcinoma of the lung has increased by leaps and bounds.

RESUMEN

1. El mejor método para el diagnóstico temprano del cáncer primitivo del pulmón es por la auscultación (véase el texto).

2. La cuestión del carcinoma primario del pulmón como resultado de la irritación de la mucosa bronquial data desde 1875 y desde entonces se ha revisado frecuentemente.

3. El término medio de duración de la vida ha aument ado desde 1914 y el carcinoma del pulmón ha aumentado a saltos.

RESUME

1. Le meilleur moyen de faire un diagnostic précoce de cancer primitif du poumon est l'auscultation.

2. Le problème des relations du cancer pulmonaire et de l'irritation de la muqueuse bronchique a déjà été soulevé en 1875 et a été l'objet de nombreux travaux depuis.

3. La durée de la vie depuis 1914 s'est accrue et le cancer primaire du poumon a augmenté par bonds successifs.

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Radiological Therapy of Carcinoma of the Lung

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The problem of lung cancer must be one of increasing concern to the medical profession. The lay public is becoming more worried and confused about it. The people do not comprehend the complexities of the problem—they know only that the number of persons who die of lung cancer has assumed alarming proportions.

The steady increase in the incidence is so clearly demonstrated in a recent report from the Pathologic Institute of Dresden-Friedrichstadt. Grosse[5] of this Institute writes of 100 year statistics. From the year 1852 to 1951, a total of 78,979 autopsies were performed. The incidence of cancer in general increased during this period, but the increase in the incidence of lung cancer was much greater. This is shown in Tables I and II.

TABLE I
GENERAL INCREASE IN CANCER
1852-1951

	Per Cent	Per Cent
Male	4.7	to 15.5
Female	12.6	to 16.5

(From Pathologic Institute of Dresden-Friedrichstadt)

TABLE II
INCREASE IN PULMONARY CANCER
(Male)

Per Cent	Per Cent	
0.3	to 5.66	—of all autopsies
6.6	to 35.5	—of total cancers in all autopsies

(From Pathologic Institute of Dresden-Friedrichstadt)

The incidence of cancer in the past century has increased 3.3 times; the incidence of pulmonary cancer has increased 18 times. Since 1930, the pulmonary cancer diagnosed in life, from the report of Grosse, has increased from 35.5 per cent to 72.8 per cent. These figures are consistent with the American experience.

The treatment of this disease is of two major types; one is surgical and the other that of irradiation, or the treatment may be a combination of the two. Let us examine briefly the results of surgical treatment. DeBakey, Ochsner and DeCamp[4] reporting on 948 cases of cancer of the lung, found that of their whole series, only 54 per cent were suitable for surgical exploration, and only 35 per cent of the cases could be resected. Some of

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Presented at the Seminar, American College of Chest Physicians, San Francisco, California, June 16, 1954.

these were palliative resections. Curative resections could be performed in only 27 per cent of the cases. These writers give the five year cure rate for all resected cases as 19 per cent. The cure rate for the whole series is 6 per cent. This is similar to the overall five year cure rates reported from a variety of clinics in this country—this figure being 5 to 7 per cent.

In the series of Jones,[8] 196 cases are reported. 39 per cent of these were clinically operable, but at surgery, only 20 per cent could be resected. It is obvious then that of the cases diagnosed and considered operable clinically, only 20 to 30 per cent at the optimum will be resectable. Of all the cases resected, about 20 to 50 per cent will survive five years.

Joseph Smart[11] of London in comparing results of surgery and of irradiation in pulmonary cancer, quotes the following:

TABLE III

		Pneumonectomies	Patients Living 5 years or more
1) Tudor Edwards	(1946)	170	5
2) Brock	(1948)	101	8
3) Sellors	(1948)	130	5
4) Mason	(1949)	202	5
	TOTAL	603	23
5 year survivals		3.8%	

(Joseph Smart, from Nat'l Tuberculosis Assn. '52)

It is evident from these figures that careful criteria for operability were not applied, and the result is as one would expect—most disappointing.

It becomes clear from the figures reviewed that the surgical cure of pulmonary cancer at this time can only be improved if the patient with this disease can be brought to the operating table before the neoplasm has extended beyond the lung. Since most cases seen in ordinary practice are too far advanced for surgery, is it possible to discern the disease in earlier stages by mass survey methods? The recent paper of J. M. McNulty[10] demonstrates clearly that this is not the case. The findings are summarized in Table IV:

TABLE IV

Persons surveyed	536,012
suspected lesions	398
proved bronchogenic carcinoma	39
cases resected	22
surviving 3 years	5

(From J. M. McNulty)

Gabriele Bondi and Vera Leites[2] of New York City report a survey on 228,375 persons. In this large series, only 184 persons had lesions which were suspected of being tumors. This is an incidence of only 0.8 per cent. Only 27 cases of previously unknown primary malignant tumor were found; 24 of these were proven by histological examination; 16 of the 24 had exploratory surgery, but only 12 had resectable tumors.

It is significant that of 22 cases picked up in a survey of 536,000 people, only five were alive and well three years later, and that of 228,000 persons, 24 neoplasms were proved and only 16 were resectable. The mass survey does not appear to bring to us lung cancer in its early stages in a significantly large per cent. This raises the question of the value of mass survey in relation to lung cancer. Most mass surveys are performed for the avowed purpose of picking up tuberculosis, thus the cost is not charged to cancer. I know of no organized plan to bear the great expense of mass surveys for pulmonary cancer. For such surveys to be effective, we know it would be necessary to repeat them at six month intervals, at least. This would be a gigantic task for any community, and, were it done, there is some doubt that the results would increase notably the resectable lesions discovered. It is evident then that until some means is found for earlier diagnosis, most of the pulmonary cancer diagnosed will have to be treated by some method other than surgical.

The usual alternative to surgery is radiation therapy. Let us examine the results of this treatment for lung cancer. Sampling the literature and picking at random reports from the period 1922 to 1937, the following table is offered:

TABLE V

Year Reported	Number of Cases	Average Survival (in months)
1922	104	6
1927	59	11
1931	52	16
1936	8	8
1937	40	10

These 263 cases survived an average of 10.2 months after treatment. This may be compared with 96 cases reported in 1922 and 1927 which were untreated and which survived an average of 5.5 months.

All of the cases included in the table above were treated with orthovoltage (200 to 250 KV). The tumor dose was, in all cases, less than cancericidal. No selection was applied and patients in all phases of inoperable lung cancer were included. The aim was primarily palliative.

Leddy and Moersch[9] in 1940 reported a series of 250 cases, 125 of which were untreated. The prognosis in all was poor because all were in an advanced state of disease. Good palliative results were achieved and a few long term survivals resulted. One patient survived 146 months, one 127 months, one for 119 months and two for over 60 months. All the cases were proved carcinomas. The survival times and palliation were far less satisfactory in the untreated series. The treatment was given with orthovoltage. Certainly the radiation therapist believes that radiation has palliative value in that it does aid in the control of pain and hemoptysis, and that it does increase survival time. There are, however, dissenting opinions. These are voiced in the literature, notably by Bloch and Bogardus[1] who summarize their results in Table VI:

TABLE VI

Duration of life (in months)	No. of patients without roentgen therapy	No. of patients with roentgen therapy
1 to 6	10	12
6 to 12	15	10
12 to 24	7	11
24 to 48	2	2
48 to 60	1	1
Patients dead	35 (75.2%)	36 (85.7%)
Patients living	2	2
Results unknown	9	4
Total	46	42

(From Bloch and Bogardus)

In the early years of radiation therapy for inoperable pulmonary cancer, the tumor dose varied from 2000 to 3500 r's. It has been shown that the cancericidal dose for this neoplasm is of the order of 6000 r's. Such dosage is difficult to deliver with ortho-voltage. The skin tolerance is usually the limiting factor. Employing multiple skin portals has helped to achieve higher dosage. Tumors of the bronchi are usually about 10 cm. below the anterior skin surface. The average antero-posterior chest diameter is 23 cm. Thus, the average bronchial tumor will be in the approximate center of the antero-posterior diameter. Using ortho-voltage, the amount of ionizing radiation delivered at this point will be much less than the approximate 50 per cent which can be delivered with 1000 KV radiation. The comparative results are seen in published results of Meredith Brown[3] summarized in Table VII.

TABLE VII

	200 KV	1000 KV
Total	66	152
Number improved	28	72
Percentage	42.	48.
Number of 9 month survivals	14	48
Percentage	21.	32.

(From Meredith Brown)

There is reason to believe that with the higher voltage, a greater measure of palliation and an increased three and five year survival may be achieved.

We are indebted to Dr. Hugh Hare[7] for the pioneer work with the Van de Graff machine. This device delivers x-rays of 2 million volt energy. Dr. Hare has treated lung cancer and added the rotational factor to his therapy procedure. Thus, he delivers supra-voltage radiation to a tumor from all directions by means of the rotating chair. With this voltage and the rotational factor it is relatively easy to deliver tumor doses of 6000 r's or more to deep-seated lung lesions. The skin reactions are no longer a limiting factor. The late results of supra-voltage, notably fibrosis, may

prove a complication of considerable import. Dr. Hare and his co-worker have ingeniously suggested that a tumor dose of about 6000 r's be delivered to inoperable lesions, to be followed after a suitable period by thoracotomy. If the lesion is found resectable the surgery is carried out. Removal of the lung would thus obviate the distressing radiation fibrosis which might ensue. Too few cases have been so treated thus far to enable us to evaluate the procedure.

The use of high energy radiation will increase notably in the next few years particularly by the availability of cobalt teletherapy units. The radiation from such units is similar in quality to that of a 2 million volt x-ray or Van de Graff machine. It should be possible to assess in the next five years, high voltage radiation by itself and in combination with surgery.

One is hopeful that palliation will be improved and the survival times lengthened. Optimism, however, is hardly justified and it is the duty of the radiologist to seek other means of radiating the ever increasing number of inoperable lung cancers. One such new approach is that devised by Hahn[6] and his co-workers. They introduced radioactive colloidal gold into the bronchial tree of experimental animals. They determined that the pick-up in the mediastinal nodes was inadequate in quantity, and was delayed too much to make it an effective modality for treatment of the metastatic lesion. The passage of silver from the bronchial tree and lung parenchyma to the regional nodes was found to be greater in quantity and more rapid than gold. They then coated the radio-active colloidal gold with silver. Intra-bronchial administration of the material has been carried out in humans suffering from advanced pulmonary cancer. Doses of the order of 25 mc. of radio-active gold have been instilled intra-bronchially. The number of cases so treated and the autopsy material so far obtained is insufficient for these investigators to assess results. It is, however, an interesting approach. Possibly by means of internal radiation, such as outlined, some measure of success may be forthcoming.

It is hoped that with treatment of inoperable bronchogenic carcinoma by means of supra-voltage radiation, and the development of technics for internal irradiation that further improvements in the end results will ensue.

CONCLUSIONS

(1) So small a per cent of the increasing incidence of lung cancer is resectable that efforts must be made to improve the treatment of inoperable lesions.

(2) Improved equipment and technics of radio-therapy may increase palliation and survival times.

(3) Internal irradiation with radio-active isotopes is a modality whose usefulness is to be explored.

RESUMEN

1. Es tan pequeño el porcentaje de cáncer del pulmón que se puede resecar que es necesario hacer esfuerzos para mejorar el tratamiento del cáncer inoperable.

2. Las mejoras en el equipo y en las técnicas de la radioterapia pueden aumentar la paliación y la sobrevida.

3. La irradiación interna por isotopos radioactivos es una modalidad cuya utilidad está por investigarse.

RESUME

1. Dans la fréquence tojours croissante du cancer bronchique, le pourcentage des cas opérables reste si limité que des progrès s'imposent pour permettre le traitement des lésions inopérables.

2. Le perfectionnement de l'équipement et des techniques de radiothérapie pourra augmenter les possibilités de traitement palliatif et de survie du malade.

3. Des irradiations internes, grâce aux isotopes radio-actifs réalisent un procédé dont l'utilisation doit être étudiée.

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Bronchial Carcinoma in Printing Workers

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1. The occurrence of pulmonary carcinoma

The striking increase in the occurrence of bronchial carcinomas during recent decades has been treated by numerous authors and to some extent also covered by myself in an earlier publication, where references on the literature previous to 1931 are to be had. In some instances no increase has as yet been noted (for example in Iceland) but otherwise there is a fairly general agreement about the presence of a considerably increased frequency of these tumors. The character of this increase, however, has been the subject of some disagreement. On the one hand it has been maintained that the increase, although considerable, should be considered as more apparent than real. The explanation offered by the supporters of this aspect is that the improved diagnostic facilities in connection with the increased average age of the population should represent the responsible factors. On the other hand there are several authors, who tend to look upon the increased frequency of lung cancer as a reality. Whilst these authors on the whole have been at a loss when attempting to account for the increase (vide infra) this fact should not *per se* be allowed seriously to impair their conclusions. For reasons developed in my paper on this subject of 1931 I am inclined to agree with those authors who believe in the increased occurrence of bronchial carcinoma as an empirically established fact.

With regard to Sweden no systematic investigation about the occurrence of pulmonary carcinoma seems to have been undertaken with exception of my own study already referred to. This study dealt with the material observed at the University of Lund during the years 1890-1930. Since this material was of limited size no conclusions as to the occurrence of lung cancer were to be made. A more comprehensive review of the Swedish material has been scheduled by us. In the meanwhile the material observed at the University of Upsala during the 20-year period 1931-1950 has been analyzed. The figures refer to all verified cases observed at the

Years	*Males*	*Females*	*Total*	
1931-35	6	8	14	together 31
1936-40	12	5	17	
1941-45	20	6	26	together 61
1946-50	22	13	35	
In all	60	32	92	

From The Medical Department (Head: Professor E. Ask-Upmark) of The Royal Academic Hospital of Upsala, Sweden.
I am indebted to Dr. Wiklund at the clinic of Crafoord in Stockholm for the use of his material, to the Swedish Union of Printing Workers for much valuable assistance and to Professor Gunnar Dahlberg of Upsala for his kind supervision of the statistical analysis.

Royal Academic Hospital and derived from the province of Upland: several other instances sent to us from other provinces have not been included.

It will be seen that the number of cases observed during the last decade is about twice the number observed in the previous decade. The difference is obvious, but it should be observed that the figures anyhow are rather small, that the number of patients observed in our hospital has been somewhat increased as well* and that the surgical facilities of dealing with pulmonary carcinoma have been available in our hospital mainly during the last decade only. Hence, we do not propose that the figures quoted above, although suggestive, are conclusive as far as the increase is concerned. It should be observed that the proportion between male and female cases is about 2:1, thus a far less preponderance for males as has been demonstrated in other statistics, and that this proportion has remained essentially unaffected throughout the 20-year period concerned.

From the point of view of medical statistics Sweden may otherwise serve as a useful test-tube, since the country is of limited size, the living conditions fairly equal and the medical registration of good standard. As far as lung cancers are concerned, however, we have in Sweden hitherto no registration of morbidity and mortality. Because of that the question whether there is, as yet, any real increase of lung cancer in Sweden cannot be answered. It may, however, be maintained that the figures quoted above for the province of Upland do by no means rule out such an increase. It may, moreover, be emphasized that statistics from Denmark, from England and from the United States make it overwhelmingly probable that we are faced with a real increase of pulmonary carcinoma. This is one of the facts we have to go upon; another is the time-honored frequency of this type of cancer in the miners of Schneeberg and Joachimsthal.

2. Why has the pulmonary carcinoma increased?

This question has been the subject of numerous investigations. Whereas there can be no doubt about the cause of the high frequency of the pulmonary carcinoma in Schneeberg and Joachimsthal—the exposure to irradiation from the uranium compounds—the increase of pulmonary carcinoma in general has so far remained rather enigmatic. There are apparently good reasons to believe in the importance of cigarette smoking, as set forth by several authors and particularly carefully analyzed by Wynder and Graham. Whilst not denying the possibility or perhaps even the probability of this carcinogenic factor there is no reason why not other possibilities should be considered as well.

One of the outstanding differences between life of today and life of 50 years ago is the increased amount of printed material available, not least so with regard to the newspapers. Their number, size and editions have increased conspicuously and the same goes with the opportunity to read

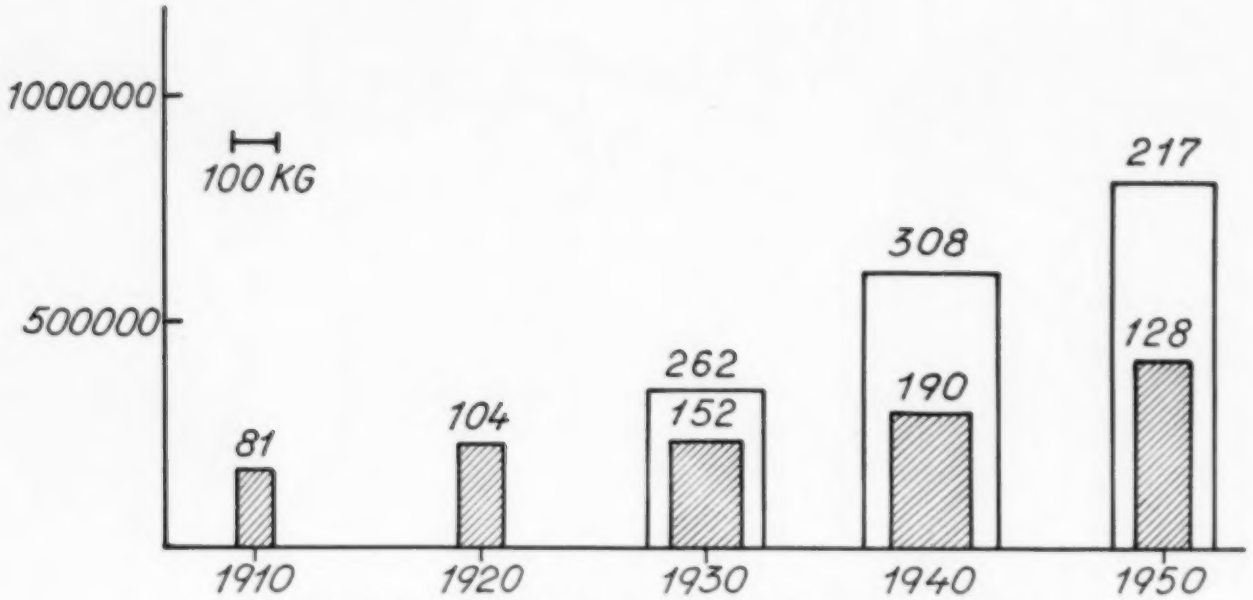
*The number of patients observed in the Medical Department was in 1931=2334, in 1941=3036, in 1950=3342. The majority of the bronchial carcinomas, or 71 out of 92, were registered in the Medical Department, whereas only eight instances were derived from the Chest Department and the rest from the Surgical Department. The Chest Clinic delivered its first case of pulmonary carcinoma in 1941.

which has been afforded the general public by the social reforms, such as the 48-hour or even 40-hour week. The average citizen has a hitherto unparalleled opportunity to get "hot news," almost smelling with printing ink. In order to substantiate this factor information has been assembled about the five top-ranking Swedish daily newspapers (Svenska Dagbladet, Dagens Nyheter, Stockholmstidninbgen, Aftonbladet, Morgontidningen). The size of their assembled edition approximates nowadays 1,000,000 copies daily. The development of this edition is reproduced in the following diagram where the vertical lines (ordinate) indicate the number of copies and the horizontal lines (abscissa) mean the assembled weight in kilograms of one sample of their yearly editions. The cross-hatched areas represent those newspapers about which information is available since 1910, the white area all five newspapers together. It will be seen that there is a continuous increase only interrupted in 1950 by the temporary restrictions of paper supply, which make the total weight of the sample of the yearly edition during 1950 less than earlier, although the editions as judged from the number of copies and represented by the vertical line are steadily on increase.

It may be presumed that the amount of printing ink is approximately proportional to the size of the individual newspaper, although differences pertaining to the type of paper and the typographical details may render this correlation not quite exact. It may, further, be presumed that on an average the same development refers to other daily papers, let alone the increasingly abundant weekly press and the book market. Finally, there is no reason why the evolution of printed material should be much different in Sweden from that in other countries, except for the temporary changes that may have been brought about by war-conditions.

We are, thus, faced on the one hand by an increased amount of printed material available to everybody, on the other hand by an increased frequency of pulmonary carcinomas. It is perfectly obvious that these two phenomena do not need to have anything in common. There is, however, some evidence to the effect that such may be the case. This evidence is represented by: 1. certain animal experiments, carried out 25 years ago in Germany, 2. an analysis of the occurrence of pulmonary carcinomas in printing workers as compared to that in the average population.

Reproduction of the drawing of one of the mice of Steinbrück



The edition of the five leading Swedish newspapers 1910-1950. Vertical lines: number of copies daily. Horizontal lines: assembled weight of one sample of the yearly edition of the newspapers concerned (about the crosshatched areas see text).

With regard to the first of these observations, Steinbrück, in 1929 painted the necks of 16 mice with printing ink. Malignant tumors ensued in eight instances: in five cases carcinomas of the lung and of the skin, in three cases neoplastic tissue in the lymphatic nodes, the liver and the spleen. This observation has to the best of my knowledge been forgotten or overlooked by all authors dealing with pulmonary carcinoma in human cases, perhaps owing to the fact that the investigation of Steinbrück was published in a veterinarian journal. A reproduction of a drawing from Steinbrück's paper will be found in the preceding picture.

As to the occurrence of pulmonary carcinoma in printing workers our attention was focused on this matter already in 1931: out of our small material of 30 male cases the profession was being registered in 25. One of these men was a typographer, aged only 31. In order to assemble a more considerable material we have, with due permission, made use of the cases published by Wiklund from the clinic of Crafoord in 1951. This monograph includes 259 cases, 23 of whom were females. If only male cases above 40 and residing in Stockholm are included, approximately 125 cases of bronchial carcinoma are to be considered. Out of these 125 instances eight were represented by printing workers, i. e., 6.4 per cent. Now, the male population of Stockholm above 40 for the corresponding period was represented by 132,000 persons. We have found that about 1500 out of these 132,000 were typographers, i. e., 1.14 per cent. If 125 males are picked out at random from the population of Stockholm above 40 this figure may be variable and should rightly be considered 1.14 ± 0.95 per cent. The maximal frequency would hence become 3.99 per cent. Since the real frequency was eight typographers out of 125 males with carcinoma — 6.40 per cent, the difference is significant. It may be added that only about 500 of the 1500 typographers are exposed to printing ink and that as far as we have been able to ascertain all eight instances are included in this group. *This would mean that the occurrence of bronchial carcinoma in typographers exposed to printing ink would be about 18 times as large as in the average population.*

Moreover, it may be mentioned, more as a curiosity perhaps, that out of the total material of Wiklund 13 were less than 40 years of age: the distribution between the sexes and between residents and nonresidents of Stockholm of these 13 cases is unknown to me, but one of this small population of 13 was a typographer from Stockholm, aged 38. This may of course be incidental, but in the light of the total material one cannot but consider the possibility of a causal relationship. Otherwise, the average age of the eight cases above 40 was 55 (ranking from 47 to 62), thus approximately the same as with the rest of the material.

It is perfectly obvious that further observations on this matter are urgently needed. Whereas several other professions may be open to the objection that the employee involved may only recently have joined the occupation, such is not the case with the printing workers. The occupational analysis should, however, pay attention to this point as well as to other things, such as the smoking habits of the workers employed. In any

material the sampling error will obviously have to be considered. It may, further, be objected that the conclusions arrived at are mainly based per analogiam: in Sweden the amount of printed material has increased tremendously and it is being presumed that such is the case also in the rest of the literate world. It would apparently be interesting to know the occurrence of pulmonary carcinomas in regions of the world where most people are analphabets. At an international congress of editors recently held in Stockholm it was maintained that the world is divided into two parts: one, reading newspapers, and another, only reading newspapers in a limited extent: it was reckoned out that the amount of paper for each citizen in the former part of the world was about 71 kilograms yearly, whereas the burden of paper, as represented by newspapers, was limited to 2 kilograms in the other part of the world for each citizen. Unfortunately, in analphabetic regions of the world the diagnostic facilities are poor.

Another objection to our thesis is the following: we do not know for certain whether the amount of bronchial carcinomas have increased in Sweden as yet, owing to a hitherto less accurate central registration of this type of tumor. There is, however, some evidence to that effect.

Among occupational factors in bronchial carcinomas the importance of chromium has been known for several years as has also the exposure to asbestos. Kennaway has mentioned the gas stokers and the gas producer men as particularly apt to develop this dreadful disease. Recently, Breslow has it that exposure to metal fumes and particles, as in welders, firemen and boilers, should increase the liability to lung cancer. The importance of uranium as exemplified by the employees of Schneeberg and Joachimsthal is particularly well known and may in the future become still more conspicuous. To these professions may, according to the present study, be added the typographers exposed to printing ink. It seems reasonable to ask for a screening by means of x-ray films of printing workers above 40, if possible every year or at least every second year and of course more often if any symptoms of a respiratory affection should appear.

SUMMARY

1. Bronchial carcinoma has increased during recent decades. This increased incidence is believed to be real more than apparent. No satisfying explanation has so far been offered although the increased consumption of cigarettes may or may not be of importance.

2. One out of several outstanding differences between life of today and life of 50 years ago is the increased amount of printed material available, not least so with regard to the number, the size and the editions of the newspapers, as well as to the opportunity to read and to get "hot news," almost smelling with printing ink.

3. If the exposure to printing ink should be of importance one ought to expect an increased incidence of pulmonary carcinoma in printing workers. The material of bronchial carcinoma in Stockholm (as published by Wiklund from other points of view) was accordingly analyzed.

4. During a certain period of time 125 cases of bronchial carcinoma were registered, eight of whom were represented by printing workers (= 6.4 per cent). During the same period of time there were 132,000 men above 40, 1500 of whom were printing workers (= 1.14 ± 0.95 per cent). The difference is conclusive from statistical point of view and will be still more overwhelming if it is remembered that only about 500 printing workers were busy with the printing ink and that, as far as could be elicited, all eight carcinomas belonged to this group.

5. Attention is called to the experiments of Steinbrück in 1929. Mice were painted on the neck with printing ink and malignant tumors was the result (in five cases carcinoma of the lung and of the skin, in three cases neoplastic tissue in the lymphatic nodes, the liver and the spleen).

6. Just as the mining workers of Schneeberg and Joachimsthal, as the laborers of the chromium industry and as those exposed to asbestos the printing workers exposed to printing ink should be considered as particularly susceptible to bronchial carcinoma. Screening by means of x-ray films should be performed of the lungs of printing workers above 40 at least once every second year and more often if any symptoms should appear.

RESUMEN

1. El carcinoma bronquial ha aumentado durante las recientes décadas. Este aumento de frecuencia parece ser real más que aparente. Ninguna explicación satisfactoria se ha podido ofrecer hasta la fecha, aunque el aumento en el consumo de cigarrillos puede o no ser de importancia.

2. Una de las diversas diferencias notables entre la vida de hoy y la de hace 50 años, es el aumento en la cantidad de material impreso al alcance de la gente. Y esto no sólo en cuanto a número y tamaño de los periódicos, sino por la avidez de poder leer "noticias calientes" en las que todavía se percibe el olor de la tinta de imprenta.

3. Si el estar expuesto a la tinta de imprenta tuviese importancia, se debería esperar un aumento en la frecuencia del carcinoma pulmonar en los impresores. El material de carcinoma bronquial en Estocolmo (según publicación de Wiklund desde otros puntos de vista) fué analizado al respecto.

4. Durante un cierto período se registraron 125 caso de carcinoma bronquial, 8 de ellos estaban representados por trabajadores de imprenta (6.4%). Durante el mismo período habían 132,000 hombres encima de 40 años, 1,500 de los cuales eran trabajadores de imprenta (1.14 ± 0.95 por ciento). La diferencia es concluyente desde el punto de vista estadístico y sería mucho más sorprendente si se recuerda que sólo cerca de 500 trabajadores de imprenta tenían contacto directo con la tinta de imprenta y que, más de lo que podría esperarse, los 8 carcinomas pertenecían a este grupo.

5. Llaman la atención los experimentos de Steinbruck en 1929. Los ratones eran pintados en el cuello con tinta de imprenta y el resultado era la producción de tumores malignos (en 5 casos cáncer del pulmón y de la piel, en 3 casos, tejido neopiásico en los ganglios linfáticos, el hígado y el bazo).

6. Tanto como los trabajadores de las minas de Schneeberg y Joachimsthal, como los obreros de la industria del cromo, y los expuestos a asbestos, los impresores que se exponen a la tinta de imprenta deben ser considerados como especialmente susceptibles al carcinoma bronquial. Los trabajadores de imprenta de más de 40 años de edad deberán ser controlados con radiografía de tórax por lo menos cada dos años o más amenudo si hay algún síntoma que lo amerite.

RESUME

1. Le cancer bronchique a augmenté de fréquence au cours de ces dernières décades. Il semble bien qu'il s'agisse d'un accroissement véritable, et non pas seulement apparent. Que l'augmentation de la consommation de cigarettes ait ou n'ait pas d'importance, il n'y a pas eu jusqu'à présent d'explication vraiment satisfaisante pour rendre compte de cette évolution.

2. L'une des quelques remarquables différences qui opposent la vie menée actuellement à celle qu'on menait il y a 50 ans est l'augmentation de la quantité d'imprimés mis à la disposition du public. Les auteurs n'incriminent pas autant le nombre, les dimensions, et les tirages des journaux que la possibilité de lire et d'avoir des nouvelles toutes fraîches, sentant presque encore l'encre d'imprimerie.

3. Si l'exposition à l'encre d'impremerie réalise un fait important, on devrait s'attendre à une augmentation de la quantité de cancers bronchiques chez les ouvriers d'imprimerie. Les auteurs ont analysé à ce point de vue l'ensemble des publications concernant le cancer bronchique, faites à Stockholm, et qui avaient été publiées par Wiklund sous un autre point de vue.

4. Pendant un certain laps de temps, ils ont noté 125 cas de cancer bronchique, dont 8 appartenaient à des ouvriers d'imprimerie, soit 6,4%. Pendant la même période de temps, 132.000 personnes, âgées d'environ 40 ans, furent examinées; parmi elles il y avait environ 1.500 ouvriers d'imprimerie (1,14%). La différence est concluante au point de vue statistique et elle est encore plus frappante si on se rappelle que parmi les ouvriers d'imprimerie 500 à peu près étaient en contact avec l'encre. Or, autant ques les auteurs peuvent en avoir eu la certitude, les 8 cas de cancer appartenaient à ce groupe.

5. Les auteurs attirent l'attention sur les expériences qui furent réalisées en 1929 par Steinbruck. Des tumeurs malignes apparurent sur le cou des souris qui avait été endui d'encre d'imprimerie. Il s'était agi dans cinq cas de cancer du poumon et de la peau, dans trois cas d'infiltration néoplasique des ganglions lymphatiques, du foie et de la rate.

6. Exactement comme les mineurs de Schneeberg et de Joachimsthal, et comme les travailleurs de l'industrie du chrome, et ceux qui sont exposés à l'amiante, les ouvriers d'imprimerie qui sont en contact avec l'encre d'imprimerie doivent être considérés comme particulièrement aptes à contracter le cancer bronchique. Il est nécessaire d'examiner par radiographie l'état pulmonaire des ouvriers d'imprimerie lorsqu'ils ont atteint

la quarantaine, au moins tous les deux ans, et plus souvent si quelque symptôme apparait.

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Case Report Section

Bronchiogenic Carcinoma Simulating Subacute Cor Pulmonale and Mediastinal Syndrome: Report of a Case.

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Bronchiogenic carcinoma giving rise to chronic cor pulmonale by infiltration of the parenchyma of the lung is not uncommon. Neither is metastasis to the mediastinal nodes unusual in bronchiogenic carcinoma. However, the rapidly progressive picture of mediastinal syndrome and subacute cor pulmonale in bronchiogenic carcinoma seems sufficiently unusual to warrant reporting.

L. M., a 41 year old salesman (No. E12023) was admitted to General Rose Memorial Hospital on November 12, 1953, with a chief complaint of dyspnea of 10 days duration. He first sought medical advice on June 17, 1953 because of vague epigastric distress of two weeks duration. Prior to that time he had been in excellent health. Nothing remarkable was found on physical examination. Routine laboratory studies were also normal except for a Wintrobe sedimentation rate corrected to 24 mm. per hour. Upper gastro-intestinal series which included fluoroscopy of heart, lungs and diaphragms disclosed no abnormality. Because of difficult family and social problems about which he expressed concern, his illness was thought to be in large part psychoneurotic. In September he noted pain in the posterior cervical and occipital regions. Repeat physical examination and routine laboratory studies again failed to disclose any abnormalities except for an elevated sedimentation rate—this time 30 mm. per hour. X-ray film of the cervical spine showed some spurring of the vertebral bodies. He was thought to have cervical arthritis and tension headaches. About 10 days prior to admission, he developed wheezing, a tight feeling in the throat and chest, severe cough productive of thick, tenacious mucous, and increasing dyspnea.

His past history revealed that he had scarlet fever and "inflammatory rheumatism" at age eight. No heart murmur was ever described. He had "yellow jaundice" at age nine—details not remembered; appendectomy in 1929; vasectomy in 1934; umbilical herniorrhaphy in 1936; and hemorrhoidectomy in 1953. Family and social history were non-contributory except that he had smoked 30 cigarettes a day for 20 years.

Physical examination revealed a markedly dyspneic, cyanotic, perspiring, well-developed and well-nourished male appearing acutely ill. His temperature was 98 degrees F., pulse 110 and respirations 18 per minute. The blood pressure was 130/80 mm. Hg. There were scattered inspiratory and expiratory sibilant and sonorous rhonchi in both lung fields and slight distention of neck veins upon rather forced expiration. The chest was clear to percussion. The heart was not enlarged to percussion. Heart sounds were partially obscured by breath sounds. No murmur was heard. No other abnormal finding was noted, though abdominal examination was not satisfactory because of dyspnea and poor relaxation. Routine laboratory studies were again normal. Chest x-ray film showed marked bilateral enlargement of the cardiac silhouette interpreted as enlargement of all chambers with early congestive changes in the lung fields from the hilar areas into the bases. On the fifth hospital day there was evidence of increased cyanosis with distention of the neck veins. There was inspiratory and expiratory coarse, wheezing rales in the left upper chest anteriorly and right lower chest posteriorly. A firm, slightly tender liver edge was felt for the first time at the level of the umbilicus. Venous pressures were recorded as 300 mm. of water in the arms and 330 mm. in the legs—patient supine. Electrocardiogram disclosed electrical alternans and right ventricular strain (Fig. 1). Careful auscultation of the heart revealed alternate variations in intensity of the first sounds. On the seventh hospital day a grade II systolic murmur was heard in the tricuspid area. Repeat x-ray film of the chest showed increased cardiac enlargement with infiltration of the right base and obliteration of the right costophrenic angle by pleural fluid. In the absence of a diagnosis, and in view of the hepatomegaly a surgical biopsy of the liver was performed on the ninth hospital day. The liver was congested and enlarged to the umbilicus but appeared smooth and grossly normal though only a small

area was visualized. The biopsy was later reported as showing hyperemia—chronic passive congestion. Following surgery he had rapid, thready pulse, but maintained normal blood pressure. He continued to do poorly despite digitalis, oxygen and respiratory stimulants, and expired the same evening.

At autopsy (A-119E) each pleural cavity contained 1000 cc. of clear fluid and the pericardial sac contained 250 cc. of hemorrhagic fluid. The most striking finding was diffuse and modular tumor infiltrations in the anterior mediastinum compressing the great vessels particularly the aortic arch and the superior vena cava. The heart together with the vessels, trachea and the tumor masses weighed 650 grams (Fig. 2). The heart was of normal size, but somewhat dilated. The epicardial surface was dull and covered with a finely nodular layer of fibrin. The valves were intact except for the aortic which showed some fibrosis. The myocardium was of average thickness, free of scars, with normal coronary arteries. In the apex of the left lung there was a 4 cm. firm, well walled-off fibrocalcific node which on section showed several areas of infiltration by tumor tissue as did the hilar nodes. On opening the bronchial system, an infiltrating tumor was found at the origin of the left upper lobe bronchus with thickening of the mucosa and marked narrowing of the lumen for a distance of 2 cm. Firm neoplastic tissue fanned out into the adjacent lung parenchyma occupying a zone 4 cm. in diameter. The right lung was free of tumor but markedly congested and edematous. The liver was studded with numerous 2 to 3 cm. nodules but none within 6 to 8 cm. of the fresh biopsy wound. The adrenals were extensively infiltrated with tumor tissue. Anatomic Findings:

1. Carcinoma, bronchiogenic, left upper lobe.
2. Carcinoma metastatic:
   a. Left lung, within and around old fibrocalcific apical node.
   b. Left pleura (scattered small nodules).

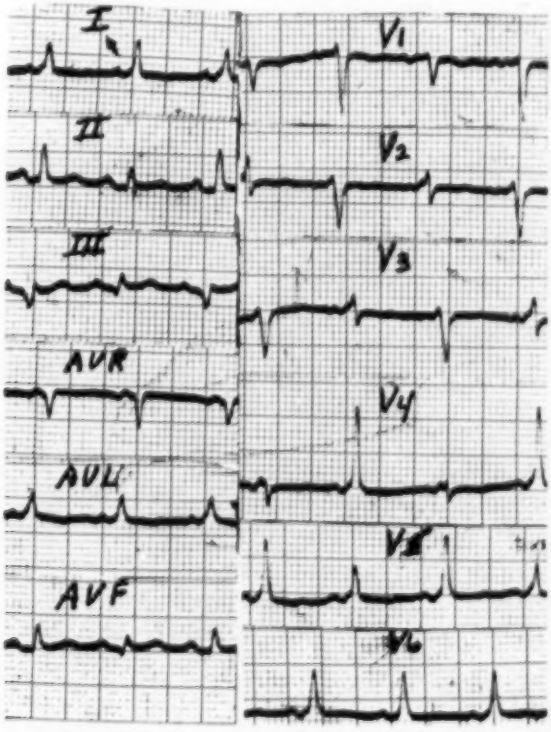

FIGURE 1: Electrocardiogram showing electrical alternans and right ventricular strain.

c. Left hilar and periaortic lymph nodes.
d. Anterior mediastinum with compression of vessels.
e. Epicardium (tumor tissue in lymphatics).
f. Liver (multiple, varying sized nodules).
g. Adrenals (extensive bilateral infiltration).

Comments

Bronchiogenic carcinoma metastasizes most frequently to the regional lymph nodes. Walther[1] found such metastases in 76.9 per cent of his 277 cases. Wegelin[2] reported 80 per cent; Willis[3] 94 per cent; and Frissel and Knox[4] the high figure of 97 per cent. Such involvement of the hilar and mediastinal nodes frequently gives rise to the superior vena cava syndrome in Mulligan's[5] experience. In the case here presented there was in addition to compression of the vena cava rather marked compression of the aorta and pulmonary vessels so that there was rapid dilatation of all chambers of the heart, a relative tricuspid insufficiency, and the clinical picture of cor pulmonale.

Production of cor pulmonale by diffuse infiltration of the parenchyma of the lung or by simple displacement of the lung by the expanding masses of tumor tissue is not uncommon in bronchiogenic carcinoma. Sufficient compression of the large pulmonary vessels by mediastinal nodes to produce this picture as in this case however, has not been frequently reported.

The relatively short duration of symptoms of bronchiogenic carcinoma has been repeatedly described. Ochsner,[6] reviewing the varying reports, quotes one author who states that the average duration of symptoms from

FIGURE 2: Heart with tumor mass constricting the great vessels. Left lung showing site of primary tumor and old fibrocalcific node. Adrenal largely replaced by metastatic tumor tissue. Nutmeg liver of chronic passive congestion with scattered metastatic nodules.

onset until death is about six months and another who found that 4 per cent of his patients had symptoms less than one month while 60 per cent had symptoms less than six months. The difficulty in dating the onset of symptoms is well shown in this case. It is certain that no symptom relating to the chest was noted longer than 18 days prior to death. The cervical and occipital pain beginning some two months earlier may well have been referred pain from the intrathoracic lesion but still emphasizes the short course. Hochberg and Lederer[7] report no symptom referable to the chest at the time of admission in 13 of their 60 cases. In seven of these, epigastric distress was the chief complaint. Whether the evanescent epigastric symptoms in this case were related to the pulmonary lesion is difficult to state. Even so the total duration of symptoms was less than six months.

This case also adds to the large number of cases reported in which the primary tumor escaped clinical and roentgenologic detection during life, death being caused by the encroachment of the metastatic lesions on vital structures. The rather typical distribution of metastatic lesions including those to the adrenals is shown.

SUMMARY

A case of bronchiogenic carcinoma is described which presented strikingly the mediastinal syndrome and subacute cor pulmonale from metastatic nodes compressing the great vessels of the mediastinum though the primary lesion escaped clinical and roentgenological detection.

RESUMEN

Descríbese un caso de carcinoma bronquigénico que presentaba un síndrome definidamente mediastinal y cor pulmonale subagudo a cause de la compresión que producían ganglios metastáticos sobre los grandes vasos del mediastino aunque la lesión primaria escapó a la búsqueda clínica y radiológica.

RESUME

L'auteur décrit un cas de cancer bronchique qui s'accompagnait d'un syndrome médiastinal et d'un coeur pulmonaire. L'origine en était la compression des gros vaisseaux du médiastin par des éléments métastatiques, alors que la lésion primitive avait échappé aux investigations cliniques et radiologiques.

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Undetected Carcinoma of the Lung with Bizarre Pain Syndrome, Associated with Separate Bladder Carcinoma and Two Dissimilar Aortic Aneurysms

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Carcinoma of the lung is ordinarily readily visualized by x-ray films. Bronchogenic carcinoma may grow within the confines of a bronchus; usually it is small, and if it breaks through the bronchial wall into the lung parenchyma, x-ray visualization should be possible.[1,2,3] Bronchoscopy might visualize an intra-luminal neoplasm in many *instances*, but there are blind areas to this diagnostic procedure. Bronchial washings may reveal tumor cells, but here, too, there are a number of diagnostic failures.

Recently, we have studied a patient who presented a bizarre symptom complex, and who was found to have an undetected bronchogenic carcinoma at autopsy. This case was studied by a group of physicians, and antemortum diagnosis was never established, although the neoplasm was large!

CASE REPORT

Mr. G. H. W. This 61 year old, white, male, married, retired architect was in apparent good health until 1946, when he developed left upper quadrant fullness and abdominal distention. He obtained relief with antacids, and subsequently duodenal ulcer was reportedly found by x-ray inspection. Indigestion continued, and was associated with mild fatigue.

On September 4, 1952, he had on onset of precordial ache different in character from his previous pain. He was hospitalized, and electrocardiographic studies disclosed acute myocardial infarction. Except for transitory right hemiparesis, possibly due to small cerebral embolus, he made a complete and satisfactory recovery on anticoagulants and bed-rest.

Family, Social and Past History: Non-contributory.

He was an incessant smoker of over 2 packages of cigarettes per day for 30 years.

Review of Systems: The patient had chronic sinusitis. He wore glasses. There was a known left renal calculus.

Physical examination was negative except the funduscopic examination disclosed some arterio-venous nicking. The nasal mucous membranes were boggy. There was partial edentula. There was mild epigastric tenderness and the left testis was small and atrophic. He stated that the digits had been clubbed since childhood. The blood findings were essentially normal.

Urinalysis was negative except 1 to 2 plus albumen and 0 to 4 white blood cells per low power field. The basal metabolic rate was minus 18. A pyelogram revealed a comparatively large calculus in the ampullary portion of the left kidney pelvis.

Gastrointestinal study showed that the duodenal cap never filled completely and was tender and overquick. No niche was seen. Impression: Probable duodenal ulcer. Numerous diverticuli of the colon were present. Cholecystogram revealed evidence of a poorly functioning gallbladder, without visible stones.

On April 1, 1953, he had a sudden onset of excruciating pain in the left leg; there was moderate pain in the right leg, and both legs were found to be pulseless. A repeat electrocardiograph showed no new findings, and it was felt that he had a saddle embolus coming from the old infarcted area of his heart. Aortic exploration revealed a large clot at the aortic bifurcation which was removed. However, he developed gangrene of the left leg, and mid-thigh amputation was performed.

The wound healed except for a small draining sinus. Despite anticoagulant drugs, on June 18, 1953, he became aphasic and again had right hemiparesis. This cleared and he returned home, walking on crutches.

On August 20, 1953, he arose from a chair and experienced a sudden ache in the precordium which lasted 15 seconds, then spread to the right anterior chest; the pain then radiated to the right lower quadrant and right pubis. On sitting, the pain dis-

appeared. Within one day, this pain appeared within one to three minutes upon assuming any position other than supine. Consultations between orthopedists, surgeons, internists, and radiologists failed to explain this syndrome. Two chest x-ray films taken after this disclosed a considerable accentuation of the hilar nodes and peculiar reticulated mottling of both lung fields. Electrocardiograms showed no new cardiac findings.

It was proposed that the syndrome might be due to an inter-atrial septal defect; in addition, there might be a large intra-cardiac clot which acted as a ball-valve.

He was rehospitalized for surveys and consultation. On the second and final entry he expired in respiratory failure after having lost more than 20 pounds, and with no evident explanation of cause of death.

Autopsy Report: The body was opened by a V incision. Cutting through the manubrium disclosed extensive neoplastic infiltration, with a yellowish friable tumor. The pericardial surface was dotted with tumor tissue, and on the posterior surface there were extensive metastases binding the pericardial sac to the posterior mediastinal structures. Opening the pericardium disclosed epicardial metastases measuring up to 2 cms. in diameter. The opened heart disclosed an inter-atrial septal defect measuring 12 mms. in diameter. In the hypertrophied left atrium there was a large scarred area to which was attached an irregular cylindrical antemortem clot measuring 8 x 2 x 2 cms., and the coronary arteries were markedly sclerotic. The excised right lung showed extensive scarring and the lower lobes were consolidated and showed, in addition, a few abscesses; the upper lobes were emphysematous. The left lung had a tumor occluding the left upper lobe bronchus, and extending into the surrounding lung tissue; it measured 4.5 cms. in diameter. There were a few metastatic nodules. There was also an old healed infarct in the lower lobe. Abdominal examination disclosed the liver to be studded with tumor nodules, and there were a number of peritoneal implants. There was a large duodenal diverticulum and numerous colonic diverticuli. The gallbladder was negative. Both adrenal glands were almost completely replaced by tumor tissue. There was a dissecting aortic aneurysm measuring 12 cms. in diameter, and just inferior to this was a saccular aortic aneurysm measuring 6 cms. in diameter. The kidneys were small, and their surface was granular and scarred. The left kidney was a shell containing purulent liquid, which also filled the entire left ureter; stones

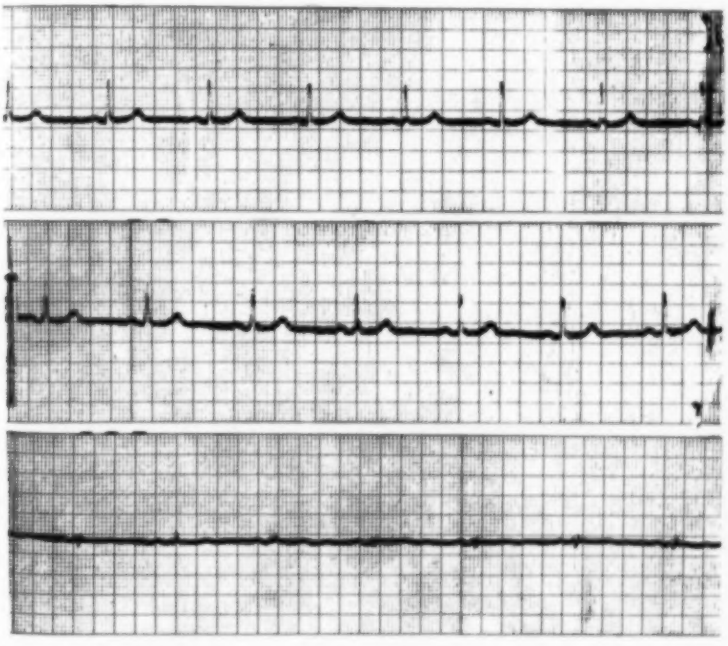

FIGURE 1: Electrocardiographic tracings taken January 15, 1951, prior to myocardial infarction.

were present in the kidney. In the bladder was another and different neoplasm measuring 4 cms. in diameter, and occluding the left ureter. The left testis was atrophic. Microscopic studies confirmed the presence of two separate malignancies, but the metastases were from the bronchogenic carcinoma.

The following is the list of final diagnoses:

Bronchogenic carcinoma, upper lobe bronchus with local metastases, region lymphnode metastases, cardiac metastases, and metastases to sternum, liver, nodes, and adrenals peritoneal surfaces.
Carcinoma of bladder, histologically distinct from the other carcinoma.
Pneumonia, broncho, severe.
Infarction, lung, bilateral, old.
Emphysema, bilateral.
Hydrothorax, bilateral.
Myocardial infarction, posterior wall, left ventricle, healed, with attached free floating antemortem clot measuring 3 x 6 x 3 cms.
Patent foramen ovale.
Dissecting aneurysm of abdominal aorta.
Saccular aneurysm of abdominal aorta.
Arterio-sclerosis, generalized.
Thrombosis of descending branch of the posterior coronary artery.

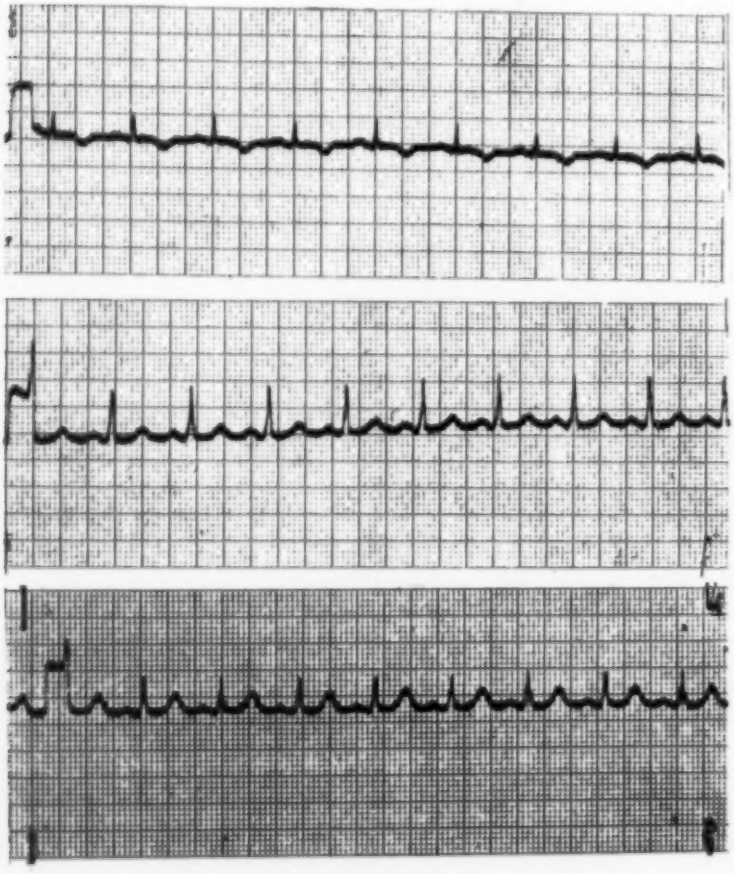

FIGURE 2: Electrocardiographic tracings taken December 12, 1952, after myocardial infarction.

Splenomegaly, due to chronic passive congestion.
Diverticulum of the duodenum.
Pyelonephrosis, left, with renal calculi.
Pyeloureter, left.
Cystic degeneration of seminal vesicles, left.
Atrophy of testis, left.
Amputation of leg, left, with sinus tract.
Decubitus ulcer.
Clubbing of the fingers.

Discussion

This case was of extreme interest because of our repeated inability to diagnose the bronchogenic carcinoma despite a "high index of suspicion" and radiological consultation. There was reason to suspect a malignancy, and yet there were no good clues that it might be intra-thoracic until the

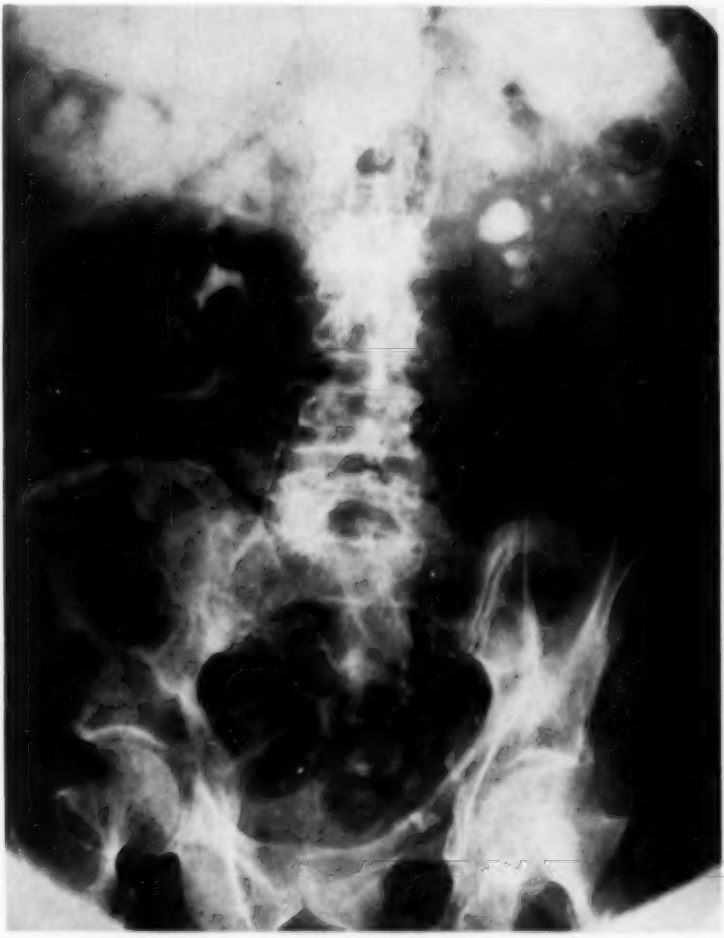

FIGURE 3: Pyelogram taken October 28, 1953, showing multiple renal calculi on the left and no dye excretion on the left.

patient was virtually moribund, when a final x-ray film showed a higher than normal position of the left diaphragm. Bronchial washings would have been tried had there been a clinical indication to do so. The peculiar reticulated appearance in both lower lung fields gave the impression of chronic passive congestion, which did exist, and the hilar areas appeared entirely compatible with this diagnosis. He had no lateral chest x-ray film, which possibly might have shown a posterior mediastinal mass.

There were two histologically distinct carcinomas: bronchogenic and bladder. The presence of two carcinomas appearing at the same time is comparatively rare.[4, 5, 6] The left renal stones seemed entirely capable of producing the urinary signs and our urological consultant felt that the patient was too ill to withstand retrograde pyelography for asymptomatic pyuria late in the clinical course. An intravenous pyelogram some months previously, did not arouse suspicions of cancer.

Of considerable interest here is the unusual pain syndrome.[7, 8] Clinical protocols were sent to various consultants here and elsewhere, and no one had encountered a similar picture. When the patient was supine or standing up, and later in his course on turning from side to side, he had an onset of severe aching, precordial pain which radiated within seconds to the right anterior chest and thence to the right lower quadrant of the abdomen. We speculated that this might be due to an intracardiac thrombus acting like a valve on changes of position. Moreover, due to the patient's small stature and life-long clubbed fingers, it was felt that he might have a congenital heart despite his lack of symptoms; an inter-atrial septal defect seemed the best possibility. At autopsy, there was a long irregular, cylindroid, attached intracardiac clot, and the inter-atrial septal defect. Despite these findings, we are still not certain as to their part in producing the pain syndrome; had there been no other lesions near the

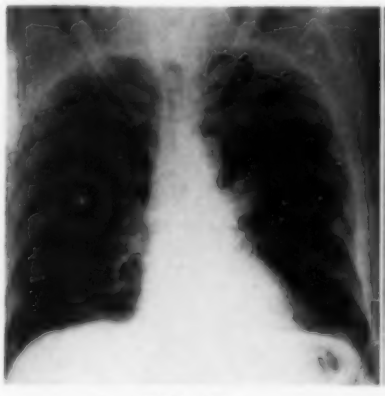

FIGURE 4

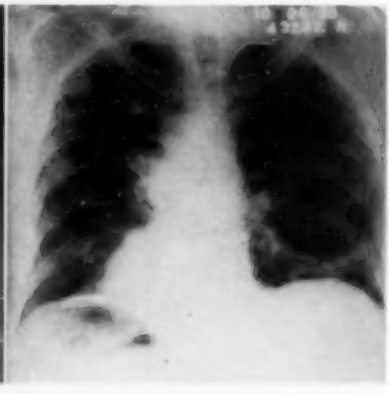

FIGURE 5

Figure 4: Chest film taken June 30, 1953, showing bizarre reticulated infiltration of both lower lung fields, with some enlargement of the hilar shadows; there was some congestive failure at this time clinically demonstrable.—*Figure 5:* This chest film taken October 26, 1953 shows an increase in the infiltration in both lower lung fields.

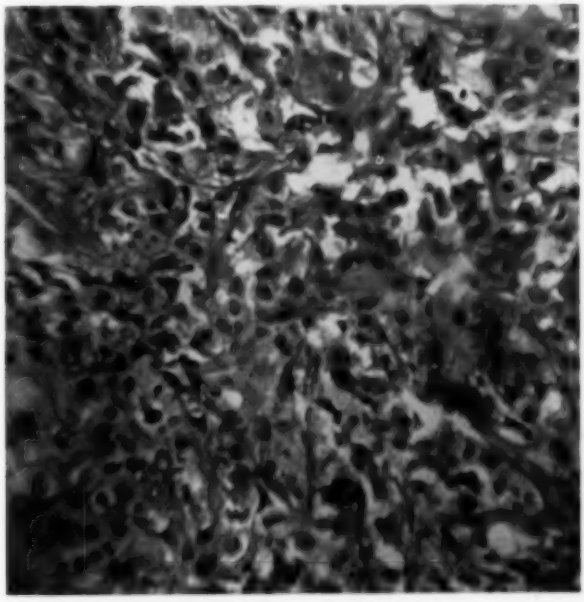

FIGURE 6: This photomicrograph shows a section taken from the cancer of the bladder.

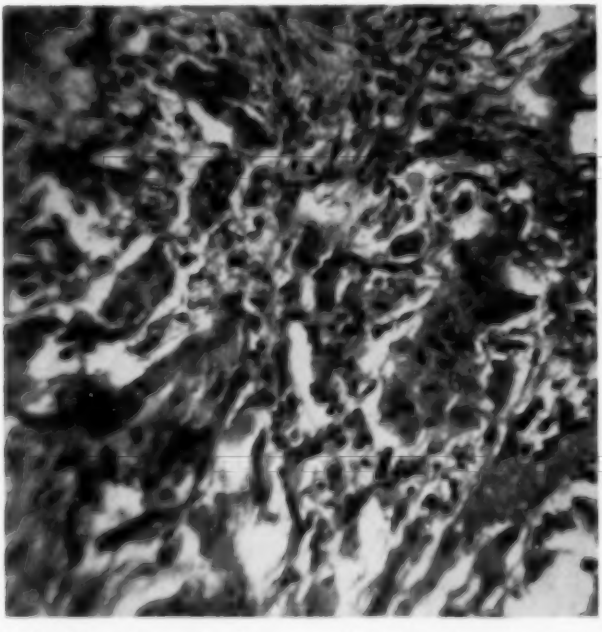

FIGURE 7: This photomicrograph shows a section taken from the cancer of the lung.

heart these ideas could have been sustained. On the other hand, there were some implants of metastatic tissue between the heart and the posterior mediastinal structures; there were some implants of cancer on the pericardium; and there was extensive invasion of the sternum with 2 x 3 x 6 cms. globular protrusion of tumor tissue from the posterior aspect of the sternum.

The presence of two separate aneurysms of the abdominal aorta is unusual. There was a fusiform dissecting aneurysm of the superior portion, and with approximately 3 cms. of markedly arterio-sclerotic aorta intervening, was a small saccular aneurysm.[9, 10, 11, 12] The clinical history did not give any good clues as to the part the dissecting aneurysm played in the pain syndrome. The pathological appearance of the aneurysms indicated that they were not of recent origin. It seems unlikely to us that this might produce the recurring pain that this patient had.

SUMMARY

1. This patient is reported for several reasons: Principally, because he had an undetected large bronchiogenic carcinoma.

2. The unusual pain syndrome is different than any encountered in our experience.

3. There were two simultaneous histologically different carcinomas; one spread widely, and the other entirely local.

4. There was an exceptionally wide variety of pathological findings, including a fusiform and a saccular aortic aneurysm only a few centimeters apart.

RESUMEN

1. Se presenta este enfermo por varias razones: principalmente, porque tenía un gran carcinoma bronquiogénico no descubierto.

2. El síndrome doloroso es diferente de cualquiera encontrado en nuestra experiencia.

3. Hubo dos carcinomas simultáneos, histológicamente diferentes; uno se diseminó ampliamente y el otro, quedó enteramente localizado.

4. Hubo una variedad excepcional de hallazgos patológicos incluyendo un aneurisma fusiforme, y un aneurisma sacular, sólo a pocos centímentos uno de otro.

RESUME

1. L'auteur rapporte une observation intéressante à plusieurs titres, mais principalement parce qu'il s'agissait d'un cancer bronchique étendu qui n'avait pu être mis en évidence.

2. Le syndrome douloureux fut très différent de tous ceux que l'auteur avait pu observer jusqu'alors.

3. Il y avait deux cancers co-existants, avec une structure histologique différente, l'un ayant donné des envahissements à distance, l'autre étant resté strictement localisé.

4. Chez ce malade, il y avait en outre une variété considérable de constatations pathologiques, et parmi elles, un anévrysme aortique fusiforme, et un anévrysme sacculaire situés à quelques centimètres l'un de l'autre.

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Pulmonary Resection for Infarction Simulating Bronchogenic Carcinoma

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Uncomplicated pulmonary infarction is one of the benign lesions in the pulmonary tree for which resection is not performed under ordinary circumstances. However with carcinoma of the lung definitely increasing in man and the curability rate remaining so low, it is little wonder that occasionally a resection will be performed unnecessarily for a benign condition simulating this dread disease. It is the purpose of this paper to review two cases where pulmonary resection was successfully performed for infarction after exhaustive preoperative studies still left one in doubt as to the correct diagnosis. Both patients had all of the clinical signs, symptoms, x-ray and bronchoscopy findings to support the diagnosis of bronchogenic carcinoma. In each instance pulmonary infarction was not considered in the differential diagnosis. In this respect, they are similar to the cases reported by Perkins and Bradshaw.[6]

Case 1: Mrs. A. H. a 64 year old woman was admitted to St. Alexis Hospital on November 22, 1950, complaining of pain in the right chest, chronic productive cough with hemoptysis, dyspnea, chills and fever. The symptoms had been progressive and of six to eight weeks duration. Physical examination revealed a white, slightly cyanotic critically ill female. There were numerous rales throughout the right lower chest. There was no evidence of phlebitis. Her blood pressure was 78/56, temperature 102.4 degrees, pulse 92 and respirations 46. She was given oxygen and put on S. R. penicillin 1 cc. intramuscularly every 12 hours and aureomycin 250 mgm. every four hours. An x-ray film of the chest revealed a localized pathological process in the midportion of the right lung which was interpreted as either a lung abscess or a

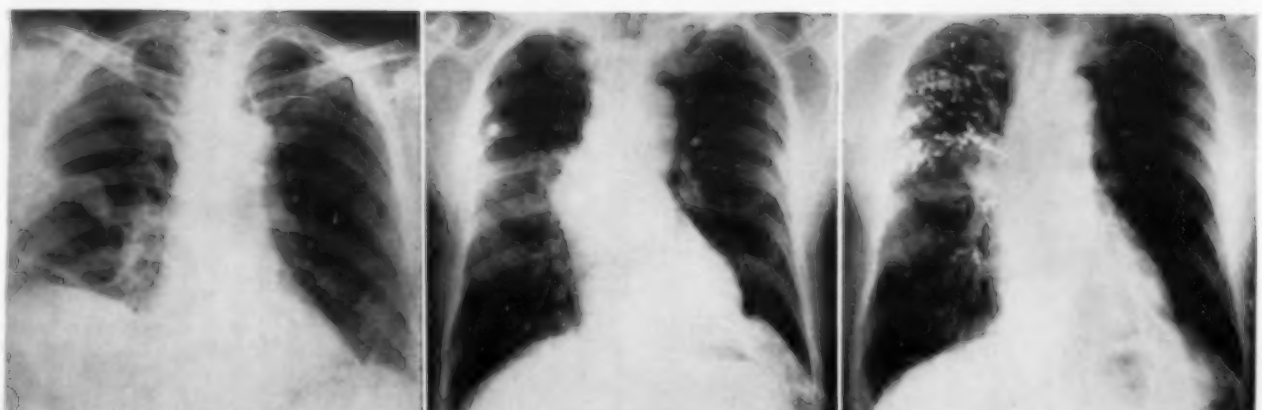

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1: Lesion in the right chest. Progressive x-ray films showed no change in the size of the mass. *Figure 2:* Roentgenogram demonstrating atelectasis of the posterior segment of the right upper lobe. *Figure 3:* Bronchogram showing a round mass near the hilum with obstruction of the bronchus to the posterior segment of the right upper lobe.

carcinoma with early cavitation (Fig. 1). Dyspnea was much relieved with the oxygen but her temperature remained between 101 and 102 degrees. At the end of two days aureomycin was discontinued and streptomycin 500 mgm. every six hours was begun along with the penicillin. Her temperature still remained elevated but there was clinical improvement. Subsequent x-ray films showed no subsidence of the pathological process. On December 8, bronchoscopy was performed which showed slight shift of the carina to the right but there was no evidence of an intraluminal lesion. It was felt that there was some narrowing of the lower lobe bronchus. Bronchial washings were negative for tumor cells. In view of the fact that neoplasm was still the best possibility, exploratory thoracotomy was deemed advisable. This was performed on December 14, 1950.

The chest was opened through a posterior lateral incision resecting the right sixth rib subperiosteally. The right lower lobe was densely adherent to the diaphragm. In the periphery of the basal segment of the right lower lobe was a firm mass approximately 4 cm. in diameter with puckering over the overlying visceral pleura. One was unable to determine whether this was a carcinoma grossly. There was another mass palpated in the superior segment of the right lower lobe and still another in the midportion of the basal segment. In view of the fact that one was unable to determine if these were malignant, a right lower lobectomy instead of wedge resections was deemed indicated. The basilar segment was gradually freed from the diaphragm. The basilar artery was isolated and tied proximally and distally with black silk. It was transfixed and cut between. The inferior pulmonary vein was isolated and treated in like manner. The superior segmental artery was isolated, clamped, cut and tied. The basilar bronchus and the superior segmental bronchus were both isolated, clamped and sutured over with interrupted black silk. The entire lower lobe was removed. The chest was then closed in layers with interrupted black silk leaving a large catheter in place for under water drainage.

Pathological Description of the Lung

The specimen in formalin consists of a right lower lobe of lung weighing 235 gms. and measuring 14 x 11 x 5 cms. About the main bronchus the tissue is roughened due to previous sectioning over an area 6 x 5 cms. The pleurae are thin and glistening except along the infero-lateral margin over an area 7 x 4 cms. where they are slightly thickened by fibrous adhesions. There is also slight thickening and puckering of the pleura in the anterior midportion. Section through this latter region reveals a rounded encapsulated mass of tissue resembling lung tissue except that it is firmer and noncrepitant and has pinkish brown cut surfaces. This mass has a maximum diameter of 2 cms. Section through the thickened pleura at the infero-lateral portion of the lung reveals another encapsulated mass which is pyramidal in shape with its base at the pleural surface and its apex pointing toward the hilum. The tissue of this mass likewise resembles lung tissue but is firmer and noncrepitant. Centrally it is softer than the previously described mass and reddish brown. The main bronchi have been previously partially opened. There is slight saccular dilation of some of the bronchi and some longitudinal ridging. A few of the bronchi contain what grossly appears to be blood clot. A pulmonary artery 6 mms. in diameter leading toward the infero-later portion of the lower lobe is filled with a cylindrical mass grossly resembling thrombus. This is not adherent. Two sections, one of thrombus alone and one of thrombus within the artery and adjacent bronchus. Beneath the pleura on the antro-inferior portion of the specimen is an ovoid mass which is encapsulated and 15 mms. in maximum diameter and similar to the infero-lateral mass previously described. One section to include pleura on two sides. Serial sections of the lung tissue reveal light pinkish brown, subcrepitant lung tissue of normal consistency except that as noted in

the previously described masses. One section. There is a small zone of atelectasis 2.5 cms. in diameter in the midlateral portion of the lobe. Microscopic diagnosis: Organizing infarcts (3) of lower lobe of right lung. Emboli in pulmonary arteries to lower lobe of right lung.

Her postoperative course was uneventful until the sixth postoperative day at which time she developed left superficial phlebitis. This gradually subsided and at the time of her discharge on the 16th postoperative day her legs were entirely normal. At no time was there any evidence of deep phlebitis. It has now been almost four years since her operation and she has remained entirely asymptomatic.

Case 2: Mr. P. S. (No. 169024) a 66 year old man was admitted to Lakewood Hospital on June 13, 1950, complaining of hemoptysis. He stated that he had been well until 24 hours before admission when he coughed up a teacupful of bright red blood. His only other symptom was a pulling sensation under the lower sternum when coughing. Physical examination revealed a normal male of stated age lying comfortably in bed in no apparent distress. His blood pressure was 110/70, with a pulse rate of 80. His respiratory rate was 20 per minute. Auscultation revealed bilateral course rales. The remainder of his examination was negative. An x-ray film of the chest (Fig. 2) showed atelectasis of the pectoral segment of the right upper lobe suggesting chronic bronchial obstruction. A bronchogram (Fig. 3) showed a lack of filling of the pectoral branch of the right upper lobe. On June 14, bronchoscopy was performed at which time blood clots were removed from the right upper lobe bronchus. Bronchial washings were obtained which were suggestive of tumor cells. Observing that there was no change in the roentgenogram and with all the evidence pointing toward the lesion in the lung being a bronchogenic carcioma, he was operated upon June 23.

The chest was opened through a postero-lateral incision by resecting the fifth rib subperiosteally. The right upper lobe was found to be involved in a process which made it look and feel like liver. Right upper lobectomy was performed by the individual ligation technique and the chest was closed in layers leaving two catheters in for under water drainage.

Pathological Examination. The specimen in formalin consists of one lobe of the lung. In the lower portion of this lobe there is an area measuring 9 x 5 cm. which is more firm than the remaining lung tissue. The cut surface is moist and bloody fluid escapes from it. No gross evidence of tumor is found.

Microscopic Description. Sections of the lower portion of the lobe reveal a marked degree of hemorrhage with some necrosis of the parenchyma. The area of necrosis is rather poorly defined and the hemorrhage extends well beyond the necrotic portion.

Diagnosis: Infarct of the lung, recent—As soon as diagnosis was established he was placed on anticoagulant therapy (Herapin). This was discontinued in three days when bloody pleural effusion developed. After thoracentesis he had no re-accumulation of fluid and the remainder of his convalescence was uneventful. In this case, with the pectoral branch of the right upper lobe bronchus blocked and bronchial washings which suggested tumor cells, there was even more evidence to support a diagnosis of bronchogenic carcinoma.

Discussion

Carcinoma of the lung may masquerade on the roentgenogram under various types of shadows. We are all beginning to become suspicious of any inflammatory lesion in the lung which does not readily clear on medical therapy. Too many patients were treated in the past and unfortunately

too many are even being treated today for an inflammatory lesion in the lung while carcinoma is the underlying cause. Antibiotics will clear the peripheral manifestations but will do nothing for the neoplasm.

Since carcinoma of the lung may imitate any of the benign pathological entities then the reverse is true. Hampton and Castleman[1] correlated post-mortem chest x-ray films with autopsy findings in 400 patients diagnosed as carcinoma of the lung. In this group, three cases of pulmonary infarction were found. They point out that clinical signs and symptoms of infarction are also present in carcinoma. It is commonly believed that infarcts are triangular with the apex pointed toward the heart but in their studies it was more apt to be oval or triangular with the apex toward the periphery. The shape of the infarct is dependent entirely upon the shape of the part of the lung it involves.

Krause,[4 and 5] found on a review of 344 instances of aseptic hemorrhagic infarction of the lung seen at autopsy at Cleveland City Hospital and correlated with the pre-mortem x-ray film findings that in only 22 per cent in which this was directly the cause of death, was the correct diagnosis made.

Pulmonary infarction occurs more often in the ambulatory patient than one realizes. It is commonly seen in the sixth and seventh decades of life and can easily be misdiagnosed unless the condition is thought of. Eleven ambulatory patients in Homans[2] series developed pulmonary infarction as the result of quiet thrombosis in the lower limbs. This same situation apparently existed in our second case although a positive diagnosis of phlebothrombosis was never made.

Although an unnecessary resection may occasionally be performed by adhering to the criteria of performing an exploratory thoracotomy for undiagnosed suspicious pulmonary lesions, many lives will be saved. Johnson, Clagett and Good[3] found that in 114 patients of a series of 384 it was necessary to resort to exploratory thoracotomy before a definite diagnosis could be made. Of these, 55 per cent proved to have malignancy. It is better to resect a lung for a benign disease than to watch the patient die of a cancer by wishfully thinking the lesion will disappear.

SUMMARY

1. Two cases of lobectomy for pulmonary infarction simulating bronchogenic carcinoma are reviewed.

2. In both cases the signs, symptoms, x-ray and bronchoscopy findings were similar to those commonly seen in pulmonary malignancy.

3. In its protean manifestations, pulmonary infarction may mimic almost any other lung disease.

4. It occurs more in the ambulatory patient than is generally realized.

5. Despite the occasional unnecessary pulmonary resection, one should not deter from exploratory thoracotomy on all undiagnosed, suspicious, pulmonary lesions.

RESUMEN

1. Se revisan dos casos de lobectomía por infarto pulmonar que simulaban carcinoma broncogénico.

2. En ambos casos los signos, los síntomas y los hallazgos radiológicos y de broncoscopía, eran similares a aquéllos que se ven comunmente en tumores malignos pulmonares.

3. En sus manifestaciones proteicas el infarto pulmonar puede simular casi todos los otros padecimientos pulmonares.

4. Ocurre más comunmente en el paciente ambulatorio de lo que-se cree.

5. A pesar de estas resecciones pulmonares ocasionales innecesarias, no debe uno dudar en hacer una toracotomía exploradora en todas las lesiones pulmonares sospechosas no diagnosticadas.

RESUME

1. Les auteurs présentent deux cas de lobectomie pour infarctus pulmonaire ayant simulé un cancer bronchique.

2. Dans les deux cas les symptômes cliniques, radiologiques et bronchoscopiques étaient ceux que l'on a l'habitude de constater dans les tumeurs pulmonaires malignes.

3. Dans ces manifestations, l'infarctus pulmonaire peut simuler pratiquement toutes les affections du poumon.

4. Il survient plus souvent qu'on ne le pense généralement chez les malades qui gardent leur activité normale.

5. Malgré la possibilité d'une exérèse pulmonaire inutile, il ne faudrait pas négliger la thoracotomie exploratrice dans tous les cas de lésions pulmonaries suspectes non diagnostiquèes.

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Carcinoma Complicating Cyst of Lung

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Cystic disease of the lung has been indicted by various writers as a precursor of carcinoma but only rarely has it been possible to prove the indictment reasonably valid. Complications of cystic disease of the lung are infection, enlargement of the cyst with compression of lung tissue, spontaneous pneumothorax, hemoptysis, perhaps bronchopleural fistula, and possibly carcinoma.

Womach and Graham[1] studied nine cases, operated on for congenital cystic disease, with particular reference to epithelial overgrowth at the site of the congenital malformations. In three of the cases there was evidence of such overgrowth, mainly masses of poorly differentiated epithelial cells tending to appear as spindle or cuboidal cells with a tendency toward invasion, but without evidence of metastasis. Though the process represented abnormal cellular growth, they did not feel justified in considering it malignant clinically. Graham[2] cites an article by Schwyter in which the relationship of congenital malformations of the lung to tumor of the lung is discussed, with eight illustrative cases, five of whom had cysts of the lung. Murphy,[3] discussing congenital cystic disease of the lung, states that at times the epithelium is cuboidal and that squamous metaplasia may be present. Under such conditions squamous cell carcinoma has been known to occur. Bass and Singer[4] reported a patient with cystic disease of the lung, who had emphysema and secondary abscess formation preceding the development of a diffuse adenocarcinoma in the same lung. Koral[5] studied 100 cases with cystic and bullous emphysema of the lungs and found seven cases with cystic emphysema who developed bronchial carcinoma, but he did not mention their relation to the cystic areas. No case of bullous emphysema, however, developed bronchial carcinoma. Moersch and Clagett[6] reported two with malignancy among 44 cases of pulmonary cystic disease. One was a 22 year old female in whom a bronchogenic cyst removed from the mediastinum showed an adencarcinoma, Grade III, arising in its wall. The other was a 36 year old male who had a cyst removed from the left thorax. In the region of the cyst wall opposite the pericardium, was a mass of soft tissue which on biopsy showed squamous cell carcinoma, Grade IV. Rogers[7] in studying the question of predisposition to pulmonary neoplasms in patients with cystic disease of the lung, states that the likelihood based on available statistical data seems remote. He found only two malignancies among persons with cystic disease, one a small adenocarcinoma discovered in the surgical specimen of a patient operated on for existing cystic bronchiectasis, the second, a rapidly fatal malignancy in the upper lobe in one with bilateral cystic disease.

At the (Kennedy) Veterans Administration Medical Teaching Group

From the Pulmonary Disease Section, Medical Service, Veterans Administration Teaching Group Hospital (Kennedy).

Hospital, 65 cases with cyst or cystic disease of the lungs have been studied, and in 24 of these the cyst was removed surgically. One operated on was found to have a bronchogenic carcinoma associated with the cyst. His case is now reported in detail.

CASE REPORT

E. S., a 53 year old white grocer was first admitted to Veterans Administration Medical Teaching Group Hospital on July 5, 1949, with a six months' history of cough productive of one-half cupful mucoid sputum daily with slight streaking of sputum for two days. He had noticed also slight feverishness and upper anterior chest pain but no wheezing. A weight loss of 14 pounds had occurred in the three weeks prior to admission. Physical examination revealed a well developed, well nourished white male, not appearing ill. The chest showed slight hyperresonance with slightly decreased breath sounds over both lung fields. Inspiratory crepitant rales were present at the left base near the anterior axillary line. The remainder of the physical examination was essentially negative except for the presence of a right inguinal hernia. The sputum was negative on concentration and culture for tubercle bacilli. The chest roentgeno-

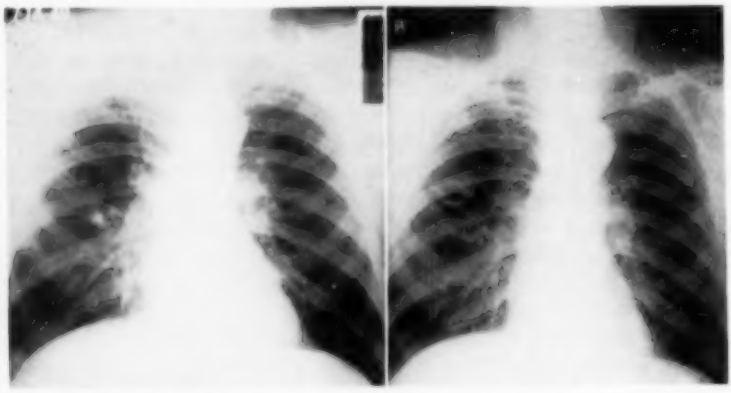

FIGURE 1 FIGURE 2

Figure 1: Chest roentgenogram made on July 14, 1949 showing the infiltrate in the right midlung field containing a small radiolucency.—*Figure 2:* Chest roentgenogram on May 1, 1950, revealing an increase in size of the radiolucency in the right midlung field.

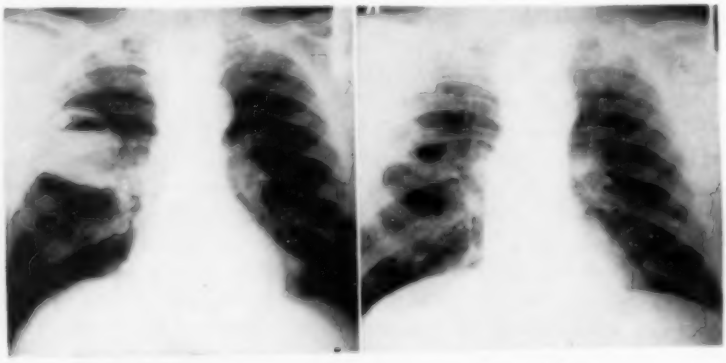

FIGURE 3 FIGURE 4

Figure 3: Chest roentgenogram on November 19, 1951, showing a marked increase in size of the infiltration and radiolucency.—*Figure 4:* Chest roentgenogram on December 6, 1951, showing considerable decrease in size of the infiltrate and radiolucency.

gram revealed an infiltrate in the right midlung field containing an area of radiolucency (Figure 1). Bronchoscopy was negative. The complete blood count was normal. The sedimentation rate was 40 mm. per hour. It was considered that the pulmonary infiltrate was an area of fibrosis, the radiolucency probably representing an emphysematous bulla. He was discharged on August 1, 1949.

He was readmitted on June 21, 1950, stating that in March 1950 he had had increased cough, fever, left chest pain with occasional pain in the right chest, weight loss, and hemoptysis of 10 days' duration. Following therapy by his local physician there was improvement in his condition though he continued to feel weak and had become more dyspneic on exertion. On this admission the physical examination revealed dullness with decreased breath sounds and crepitant rales at both bases posteriorly. The prostate showed enlargement of the lateral lobes. The sputum was negative, on concentration and culture, for the tubercle bacilli, and for fungi. Bronchoscopy was again negative, and no tumor cells were found in the bronchial aspirations. The chest roentgenogram showed a slight increase in the size of the radiolucency (Figure 2). The tuberculin and histoplasmin skin tests were positive. The coccidioidin skin test was negative. There was some decrease in size of the radiolucent area with bedrest only. Chloromycetin and penicillin caused no further improvement. It was considered that he had a cyst of the lung which intermittently became infected. He was advised to have a bronchogram but refused so he was discharged July 26, 1950.

He was readmitted nine months later on May 25, 1951, with an anterior myocardial infarction which occurred on the morning of admission. A chest roentgenogram showed a large infiltrate in the right midlung field containing a radiolucency with an air fluid level (Figure 3). He was treated for the myocardial infarction from which he made an uneventful recovery. He received several courses of terramycin for infection in the cyst with a decrease in size of the cyst and of the surrounding inflammation (Figure 4). On December 7, 1951, a wedge resection of the involved area was performed by Dr. Felix Hughes on the assumption that the lesion was an infected lung cyst. On pathological examination a squamous cell bronchogenic carcinoma was

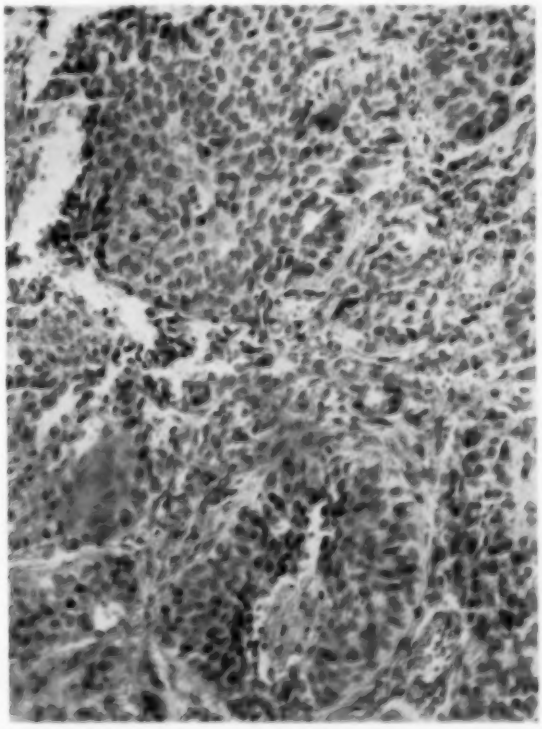

FIGURE 5: Photomicrograph from the tumor mass.

found, at the periphery of the cavity, invading the lung but with apparently no invasion of the lymphatics or blood vessels (Figure 5). Because an inadequate excision for a bronchogenic carcinoma had been performed, the patient also was treated with deep radiation therapy to the right chest, receiving 6,075r over a period of 33 days. He was discharged from the hospital on January 15, 1952.

Three months later he was recalled for re-examination at which time he stated that he had had an increasingly severe cough for two months and easy fatigability. Physical examination revealed no abnormal findings except a wheeze through both lungs which partially cleared with coughing. The chest roentgenogram showed fibrosis around the area of the horizontal fissure which was displaced upward and a diffuse haziness at the right base. Bronchoscopy revealed moderate fixation of the carina and right primary bronchus. There was firmness around the upper lobe bronchus, but the mucosa was intact. No tumor cells were found in the aspirated material. He was treated with penicillin for one week before discharge. Chest roentgenograms in July and November 1952 showed no change from the roentgenogram made in April. In November he was asymptomatic with no evidence of cancer in the lung or elsewhere.

He re-entered the hospital on April 6, 1953, stating that three weeks before this admission he had had bronchopneumonia and had been treated with penicillin by his physician. He continued to have right chest pain with wheezing, non-productive cough, and increased dyspnea on exertion. He was afebrile on admission with no evidence of pneumonia or metastasis. The chest roentgenogram showed no changes from previous films, and a radiologic survey of bones failed to reveal evidence of metastasis. He was discharged with his bronchitis improved after penicillin therapy.

On June 3, 1953, he was readmitted to the hospital with signs of mental confusion, and the chest roentgenogram showed an increased density in the right chest. A bronchoscopy revealed a slightly raised lesion in the right main stem bronchus. It was considered that he probably had a local recurrence of the tumor and possibly a metastatic spread to the brain.

Discussion

The above report tells of a case of bronchogenic carcinoma unexpectedly found in the wall of a cyst of the lung. Bronchogenic carcinomata usually arise in areas bearing no relation to evident malformations of the lung. It may arise coincidentally with a cyst by forming a ball-valve mechanism in a bronchus. In our case, however, the carcinoma was found to arise directly from the wall of the cyst, which, with the history, indicates that the tumor was a complication of the cyst. The cyst had been known to be present for two and one-half years, and the findings of a small carcinoma in the wall of the cyst, without evident metastasis at the time, makes it unlikely that the tumor had existed during the entire period the cyst was known to be present. It is possible, however, that the tumor arose from neighboring structures and invaded the cyst wall although this seems unlikely from examination of the specimen. Possibly cases with repeated infections of the cyst have a higher incidence of malignant degeneration. At any rate, the proved possibility of malignant degeneration is another indication for removal of lung cysts whenever possible.

SUMMARY

A case is described in which a small bronchogenic carcinoma was found in the wall of a long standing pulmonary cyst. The possibility of malignant degeneration in the wall of a cyst forms another indication for removal of these cysts whenever feasible.

RESUMEN

Se describe un caso en el que un pequeño carcinoma bronquiogénico de la pared fué encontrado en us quiste pulmonar de larga duración. La posibilidad de degenaración maligna en la pared de un quiste constituya una indicación para la extirpación de estos quistes cuando sea posible.

RESUME

Les auteurs rapportent une observation dans laquelle un petit cancer bronchique se trouvait dans la paroi d'un kyste pulmonaire existant depuis longtemps. La possibilité de la dégénérescence maligne de la paroi d'un kyste constitue une indication de plus pour pratiquer l'extirpation de ces lésions quand elles sont constatées.

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Spontaneous Pneumothorax As a Presenting Feature of Primary Carcinoma of the Lung

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Spontaneous pneumothorax may occur in advancing carcinoma of the lung due to extension of the disease to the pleura and rupture of the membrane. The pleural space soon fills with fluid in which tumor cells are often demonstrable. This type of pneumothorax is quite familiar and, as a rule, there is little difficulty in determining its origin. Recently the writers encountered two instances of spontaneous pneumothorax in previously apparently healthy individuals, presumably due to rupture of subpleural blebs characterizing, so-called, idiopathic or benign spontaneous pneumothoraces. Not realizing at first that carcinoma may be associated with spontaneous pneumothorax of a similar nature, there was some delay before the correct diagnosis was finally made. In a third patient pneumothorax occurred in the presence of a carcinoma, but the air absorbed spontaneously without the usual sequellae of pleural fluid and metastases. These experiences served to emphasize the importance of keeping in mind the possibility of underlying malignancy of the lung in all patients of the cancer age who sustain what may appear to be simple spontaneous pneumothoraces.

Case 1. M. G., a 45 year old white male was admitted to Montefiore Hospital on March 14, 1951 complaining of chest pain, fever and nonproductive cough. Ten days

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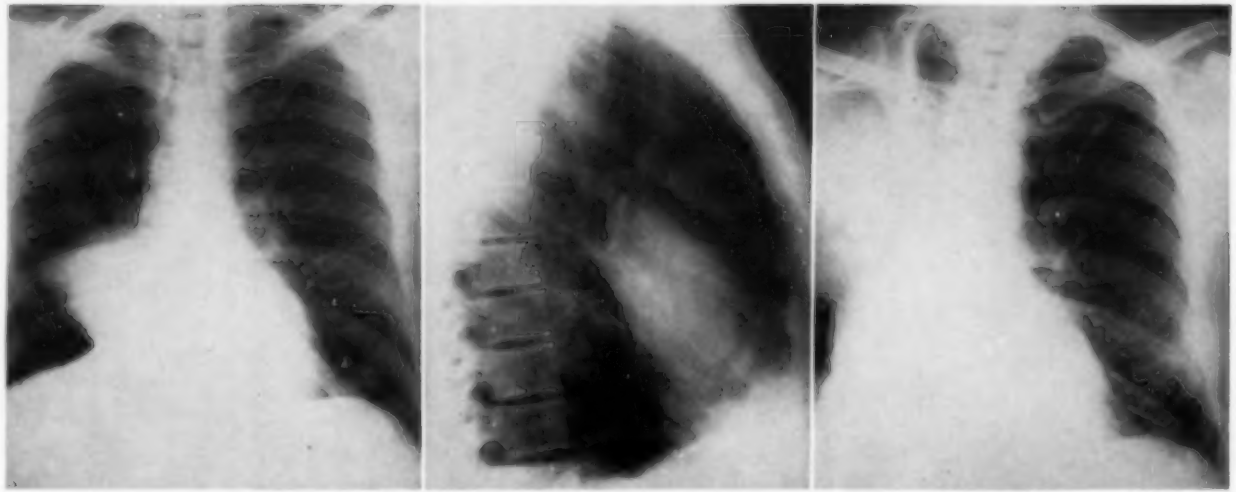

FIGURE 1A FIGURE 1B FIGURE 1C

Figures 1A and B.—(CASE 1). Spontaneous pneumothorax in a man of 45 which was later found to have been caused by a bronchiogenic carcinoma. Chest x-rays, PA and right lateral, show a pneumothorax on the right side with complete collapse of the upper and middle lobes and partial collapse of the lower lobe. *Figure 1C.*—(CASE 1). Chest x-ray 9 months later after right pneumonectomy. Resected lung revealed squamous cell carcinoma. Patient well two years after the operation.

before admission to the hospital he experienced a sharp pain in his right lower chest during a bout of coughing. Physical examination showed him breathing rapidly but not in distress. The percussion note on the right was impaired and there were diminished to absent breath sounds and "creaking" rales over that side of the chest. No other physical abnormalities were noted except for widespread psoriasis. Noteworthy in the past history was the fact that he had had periodic chest x-ray films following a seizure of bronchopneumonia three years previously and no abnormalities were found at any time. A chest x-ray film on admission to the hospital revealed right-sided pneumothorax with complete atelectasis of the upper and middle lobes and 50 per cent collapse of the lower lobe which appeared to be hyperaerated. The mediastinum was not displaced; the left lung was uninvolved (Figs. 1A and B). Examination of the sputum failed to reveal acid fast bacilli. Other laboratory tests were noninformative.

Repeated attempts to reinflate the right lung by needle aspiration of air were unsuccessful. A chest x-ray March 27, 1951 revealed a small amount of fluid at the right costophrenic sulcus; otherwise, no changes were noted. Because of the failure of the right lung to reexpand, bronchoscopy was done April 4, 1952 which revealed the trachea deviated to the left; the carina, normal. The orifice of the right upper lobe bronchus was almost completely occluded by friable tissue which protruded into and partially obstructed the main bronchus. Thick pus was found exuding from the stenotic upper lobe orifice. A biopsy obtained from the right upper lobe bronchus revealed squamous cell carcinoma.

On April 23, 1951 a right exploratory thoracotomy was done. The upper and middle lobes were completely atelectatic. The lower lobe was emphysematous and could be deflated with difficulty. A few subpleural blebs were noted. A hard mass about 3 cm. in diameter could be palpated in the hilum of the upper lobe. There was no evidence of hilar or pleural involvement; the lymph nodes were small, soft and anthracotic. Pneumonectomy was done without difficulty. Postoperatively, because of persistent fever, some pleural fluid was aspirated and found to contain hemolytic Staphylococcus aureus and Streptococcus gamma sensitive only to aureomycin. There was no evidence of bronchopleural fistula. Thoracotomy and drainage followed by thoracoplasty obliterated the pleural space. He has now been followed for 24 months, has gained 18 lbs. in weight and is asymptomatic. There is no evidence of recurrence of the carcinoma (Fig. 1C).

The resected lung revealed a cauliflower-like mass 2.5 cm. in diameter protruding into the right upper lobe bronchus. The tumor had extended through the bronchial wall into the adjacent parenchyma partially compressing the main bronchus. Beyond the tumor mass thick pus could be expressed from the upper lobe. The lower lobe was emphysematous and contained subpleural blebs. Histologic examinations of the bronchus revealed an infiltrating squamous cell carcinoma. Sections of the upper lobe showed widespread areas of pneumonia. There was no carcinomatous involvement of the hilar lymph nodes or main bronchus at the site of resection.

Comment: Until bronchoscopy was performed for what was considered a nonexpanding right lung following spontaneous pneumothorax, carcinoma of the lung had not been suspected. The pneumothorax was most likely due to rupture of a subpleural bleb in the lower lobe, the site of obstructive emphysema found at operation. The lung rupture was not due to perforation and extension of the carcinoma into the pleural cavity.

Case 2. F. M., a 53 year old Puerto Rican school teacher in apparently good health was suddenly seized with rightsided chest pain, shortness of breath and, shortly thereafter, nonproductive cough. He remained at home for one week under the care of his private physician until admission to the Morrisania City Hospital, February 27, 1947. Physical examination revealed a well developed, well nourished white male breathing rapidly but not in acute distress. The temperature was 100°, pulse 96 and blood pressure 130/90. The right side of the chest appeared fuller than the left and lagged on respiration. The percussion note was hyperresonant and auscultation revealed absent breath sounds. The left side was normal. The remainder of the physical examination was negative. A chest x-ray film taken the day of admission revealed the right lung collapsed to one-half of its size, suspended from the apex by broad adhesions. The heart and trachea were displaced to the left (Fig. 2A). Examination of the sputum failed to reveal acid fast bacilli. Other laboratory studies were within normal limits.

Thoracentesis was performed with the removal of 200 cc. of air. The initial readings were +3 —4; following the withdrawal of air the readings were 0 —6. After cough the intrapleural pressure returned immediately to +3 —4, indicating the presence of pleuropulmonary fistula. Air was aspirated from the right pleural cavity periodically in amounts ranging from 800 to 1,000 cc. but the lung showed only slight evidence of reexpansion. Water-sealed catheter drainage was instituted but it also failed to pro-

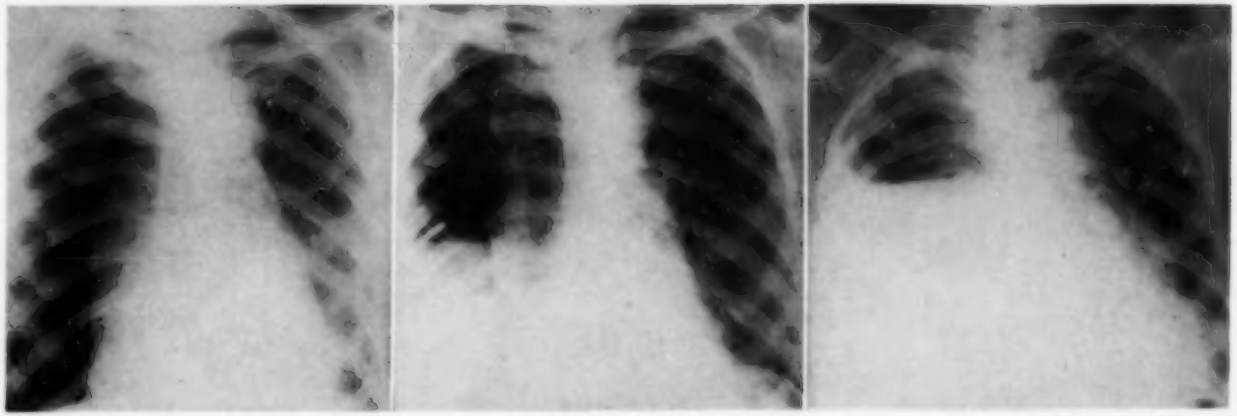

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2A.—(CASE 2). Spontaneous pneumothorax in a man of 53 which was later found to have been caused by an anaplastic carcinoma. Chest x-ray shows an almost complete right-sided pneumothorax, except for broad apical adhesions suspending upper lobe. *Figure 2B.*—(CASE 2). Two months later; draining catheter in situ; fluid now occupying lower third of pneumothorax space. *Figure 2C.*—(CASE 2). Two months later. Fluid now occupying lower half of pneumothorax space; scalloped edge of parietal pleura a biopsy of which revealed anaplastic carcinoma.

mote reexpansion of the lung (Fig. 2B). A collection of clear yellow fluid appeared in the right pleural cavity following the catheter drainage.

In view of the persistent leakage of air from the lung and the presence of adhesions at the right apex, closed intrapleural pneumonolysis was done on May 31, 1947 with the hope of sealing the fistula by releasing the suspended lobe. The visceral and parietal pleura were found to be thin and glistening, the lung parenchyma appeared normal. The site of air leakage could not be visualized. Dense apical adhesions were encountered. The right upper lobe could be freed only partly. One week following pneumonolysis the fluid in the pleural cavity increased and at this time was found to be bloody. It was considered traumatic in origin. Repeated aspirations of thick blood were necessary to relieve dyspnea. Thoracotomy was finally done June 6, 1947 under local anesthesia to improve drainage and to avoid aspiration of the pleural contents through the fistula into the left lung. Pleural biopsy at this time revealed thickened fibrous tissue infiltrated with anaplastic carcinoma. The malignancy appeared highly undifferentiated and was interpreted as a metastatic lesion from a lung carcinoma. Subsequent x-ray films revealed widespread metastatic deposits in the right pleural cavity

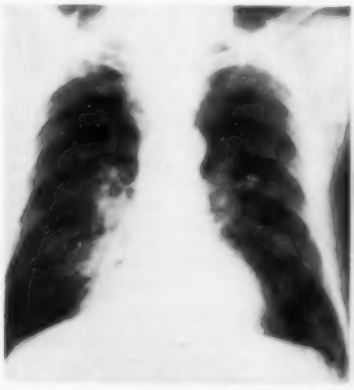

FIGURE 3A

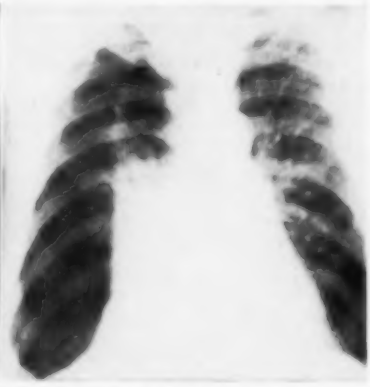

FIGURE 3B

Figure 3A.—(Case 3). Spontaneous pneumothorax complicating a known adenocarcinoma of the lung. Chest x-ray shows irregular density in right lower lobe. *Figure 3B.*—(Case 3). Six months later chest x-ray shows a right-sided pneumothorax with complete collapse of the lower lobe and partial collapse of the upper and middle lobes.

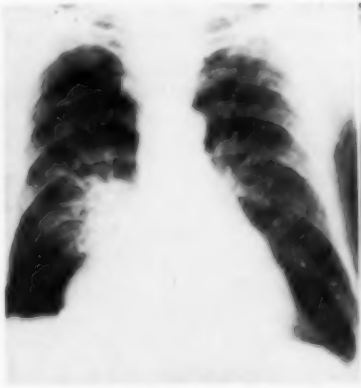

FIGURE 3C

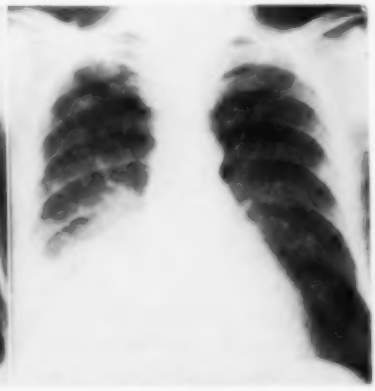

FIGURE 3D

Figure 3C.—(Case 3). One month later chest x-ray reveals partial reexpansion of the lung and a small pleural effusion at base. *Figure 3D.*—(Case 3). Three weeks later chest x-ray reveals complete absorption of the pneumothorax with residual pleural reaction.

(Fig. 2C). His course was downhill and he died on July 6, 1947. Postmortem examination could not be obtained.

Comment: This patient developed spontaneous pneumothorax, the disease in the lung being obscured by the pulmonary collapse. Not until three months after admission to the hospital did a carcinoma become evident. Pneumonolysis, which had been performed in an attempt to seal a bronchopulmonary fistula probably resulted in disseminating metastases into the pleural cavity. Bronchoscopy done early might have disclosed the presence of the neoplasm and permitted surgical exploration.

Case 3. B. R., a 51 year old white male was admitted to the Montefiore Hospital March 26, 1951 complaining of dyspnea, cough and weight loss. In September, 1950 he had noted bloody sputum and at this time a chest x-ray film revealed an irregular density in the right lower lobe adjacent to the heart (Fig. 3A). Clubbing of the fingers and enlarged liver were also noted. He refused further care and did not consult his physician until February 12, 1951 when he developed shortness of breath, chest pain and swelling of the lower extremities. A chest x-ray film now revealed right-sided pneumothorax with marked collapse of the right middle and lower lobes. An x-ray film March 8, 1951 revealed partial reexpansion of the lung and a small amount of fluid at the right costophrenic sulcus (Figs. 3B and C).

On admission to the Montefiore Hospital physical examination revealed a chronically ill man. A small firm nodule was palpable in the right supraclavicular area. The right chest was hyperresonant with distant breath sounds audible over the upper half. The liver edge was felt four fingerbreadths below the costal margin. There was edema of both lower extremities. A chest x-ray film at this time revealed complete absorption of the air from the right pleural space and small pleural effusion at the base partly obscuring a mass in the right lower lobe (Fig. 3D). Bronchoscopy revealed an infiltrative lesion in the right lower lobe bronchus extending proximally to the orifice of the middle lobe bronchus. Biopsy revealed the presence of adenocarcinoma. The patient suddenly expired on April 23, 1951. Postmortem examination was not obtained.

Discussion

Spontaneous pneumothorax may occur in advanced carcinoma of the lung from necrosis of the pleura by an invading tumor. Under such conditions the pneumothorax is soon complicated by carcinomatous involvement of the pleural cavity with the formation of a serous or hemorrhagic effusion in which tumor cells can often be demonstrated. Occasionally infection supervenes with the production of pyopneumothorax. When the aforementioned occur in the course of known pulmonary malignancy the diagnosis can be readily made. Even when an individual, especially one of advanced age, presents himself for the first time with spontaneous hydro- or hemopneumothorax the possibility that one may be dealing with an underlying carcinoma is also recognized. The cases published of pulmonary carcinoma associated with ruptured lung belong in this category.

It is well to bear in mind, however, that spontaneous pneumothorax may occur at any stage of a carcinoma of the lung as a result of rupture of a portion of the lung uninvolved by tumor. Under such conditions carcinomatous involvement of the pleural cavity may not occur, fluid may not form and the pneumothorax may absorb spontaneously. If pneumothorax of this type is encountered in the early stages of the carcinoma, when the patient is still in good health, the picture may simulate the benign or idiopathic variety and the underlying disease may not be recognized.

The site of rupture may be in a subpleural vesicle in an area of obstructive emphysema or in a pre-existing emphysematous bleb adjacent to a pulmonary scar. The reason why this type of pneumothorax is rare is partly explained by the fact that obstructive emphysema due to carcinoma

of the lung is a transient phase and soon progresses to complete bronchial obstruction and atelectasis. The rarity of spontaneous pneumothorax in carcinoma of the lung is well brought out in a recent study by Korol.[2] In a report of 10 cases developing in middle-aged war veterans with cystic emphysema, not a single instance of spontaneous pneumothorax was encountered. In a number of the cases the cystic changes in the lung were mistakenly diagnosed as pneumothorax. In contrast to the rarity of spontaneous pneumothorax in primary carcinomas of the lung, a number of reports of the occurrence of the accident in metastatic sarcoma of the lung have been described.[3, 4, 5, 6] In several, pleuropulmonary fistula developed in a necrotic subpleural nodule. In others, interstitial pulmonary emphysema and rupture of a subpleural bleb may have been the cause.

In Case 1 the excised lung revealed complete atelectasis of the upper and middle lobes and obstructive emphysema of the lower lobe due to the carcinoma. The pneumothorax could have resulted from rupture of an emphysematous bleb in the distended lower lobe. A similar surgical specimen was described by Cohen.[7] In his case the resected right lung also showed atelectasis of the upper and middle lobes and obstructive emphysema of the lower due to carcinoma of the main bronchus. The roentgen appearance of the lung following diagnostic pneumothorax, induced preoperatively in his patient, resembled closely that noted in this case.

The site of the lung rupture which caused the pneumothorax in Case 2 could not be definitely established since postmortem examination was not obtained. The nature of the lesion was not suspected until pleural biopsy, obtained three months later at the time of thoracotomy and drainage, revealed malignancy. It was our impression that the carcinomatous implants of the pleural cavity resulted from the intrapleural pneumonolysis. Had a neoplasm been suspected, bronchoscopy performed earlier might have disclosed the tumor and prompted surgical exploration.

In Case 3 spontaneous pneumothorax occurred in the presence of known malignancy of the lung. The pneumothorax absorbed spontaneously. It demonstrated again that spontaneous pneumothorax need not be caused by extension of the tumor. Surgery in this case was contraindicated because of widespread metastases. The small collection of pleural fluid noted is frequently found in instances of nonexpanding lung, especially after repeated thoracentesis or long-continued water-sealed drainage with an indwelling catheter. As is well known, effusions occur also in the presence of nonexpanding lung if a high negative intrapleural pressure exists. The cases of spontaneous pneumothorax cited in this report, as well as those following other causes, as reported elsewhere,[9] serve to emphasize the importance of bronchoscopy in all cases of nonexpanding lung before other forms of treatment are instituted.

CONCLUSIONS

Spontaneous pneumothorax may develop in the presence of a carcinoma of the lung as a result of rupture of a subpleural bleb in an area of obstructive emphysema as well as a result of invasion of the pleura by the malignancy. The former type of pneumothorax is rare. If such a pneumothorax occurs early in the disease, the picture may resemble that en-

countered in the benign or idiopathic variety. Lack of familiarity with this eventuality may cause unnecessary delay in arriving at a diagnosis. Pulmonary malignancy should be suspected if an individual of the cancer age develops spontaneous pneumothorax, especially if the latter is associated with a nonexpanding lung. The occurrence of spontaneous pneumothorax in a case of carcinoma of the lung does not preclude exploration and resection.

RESUMEN

El neumotórax espontáneo, puede desarrollarse en presencia de un carcinoma del pulmón como resultado de ruptura de bula supleural en una área de enfisema obstructivo así como resultado de la invasión de la pleura por el proceso maligno. La primera forma de neumotórax, es rara. Si tal forma ocurre al principio de la enfermedad, el cuadro puede asemejarse a la forma beningna o idiopática de la enfermedad. La falta de familiaridad con una posibilidad tal, puede resultar en retardo en llegar al diagnóstico. La neoplasia maligna pulmonar, debe sospecharse si un individuo en la edad en que el cánceres frecuente, presenta neumotórax espontáneo, en particular si éste está asociado con pulmón no expandible. Le presencia de neumotórax espontáneo en un caso de carcinoma del pulmón, no interfiere con la exploración y la resección.

RESUME

Au cours du cancer pulmonaire, le pneumothorax spontané peut être dû à la rupture d'une bulle sous-pleurale dans une zone d'emphysème obstructif, aussi bien qui a l'extension du processus malin à la plèvre. Cette première forme de punemothorax est rare. Si elle survient précocément au cours de la maladie, le tableau clinique peut prendre l'aspect de celui qui caractérise le pneumothorax bénin ou idiopathique. Si on n'est pas familiarisé avec une telle éventualité, on risque de perdre un temps précieux avant d'arriver au diagnostic. Il faut suspecter le cancer du poumon lorsque survient un pneumothorax spontané chez un individu qui a atteint l'âge habituel du cancer. Ce diagnostic doit être spécialement pris en considération si le poumon n'a aucune tendance á l'expansion. La survenue d'un pneumothorax spontané au cours du cancer pulmonaire ne doit pas éliminer la thoracotomie exploratrice et l'exérèse.

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Editorial

OUR WAR ON LUNG CANCER

The toll of lung cancer continues to rise steadily. Its deaths are now estimated to be twelve-fold that of the first quarter of this century and in the next quarter it is expected to exceed that of all other cancers combined. The present toll from all cancers in this country is about 225,000 deaths per year. At the present rate of increase, in about another decade deaths from lung cancer are likely to rise to above 100,000 per year. This is the appalling challenge, perhaps the greatest to modern medicine.

Pulmonary experts are in the foreground of this struggle. It is up to them to meet this challenge. Most of us are well aware of this. Certainly there is no need to remind us of the very discouraging facts in the present state of our battle. The ever increasing number of tragedies we witness force upon us a realization of our helplessness in preventing them. The challenge is thus brought home to us daily and the ominous forecasts of the rising tide fill us with a deep sense of frustration.

Why is there no evidence of more concerted action among chest physicians to meet this challenge? Perhaps because we are divided into camps holding opposite views as to the manner of conducting our attack. On the one hand are the pessimists who have lost all hope for early diagnosis and treatment by methods now available. They have practically resigned themselves to waiting for a biological test of early malignancy and for a chemotherapeutic agent which will arrest its growth. On the other hand are the optimists who still believe that early diagnosis by available methods is possible and that cure by early surgery is feasible. They are convinced that our diagnostic and surgical possibilities are not being adequately utilized. They continue to argue for earlier diagnosis mainly through exploratory surgery.

To this writer, both of these attitudes seem erroneous. The pessimism of the former amounts to defeatism born of frustration and is unworthy of our old clinical traditions. The optimism of the latter is not supported by current clinical experience and suggests an unwillingness to accept or an ignorance of realities. We cannot sit idly by just waiting. We must continue to exert every conceivable effort to reduce the toll of lung cancer until current research has produced the test for early diagnosis and the chemotherapy of the disease. On the other hand spending time in recriminations and disputes as to placing the blame for delayed exploration of more and more patients in futile. We cannot reduce significantly the mortality of lung cancer by performing more exploratories.

What is required is more and earlier diagnoses. We too are optimistic in the belief that these can be accomplished, provided they are made the goals of a well planned campaign for concerted action on a grand scale.

Warranting such an optimistic outlook are the following facts:

(1) The lung is an organ most accessible to exploration by x-ray visualization.

(2) Its airways are to a great extent accessible to direct endoscopic visualization.

(3) It is accessible for obtaining specimens for cytologic examination.

(4) Experience has shown that most cancers of the lungs present a slow and more chronic growth than we previously had reason to believe.

(5) The incipient phase has the longest duration. Observations suggest that the biological characteristics of incipient malignancy may differ fundamentally from those of advanced stages; and even that a biologically inactive phase exists before malignant cells at the site of origin grow invasively.

To take full advantage of these favorable circumstances we must now begin our campaign with a revision of the concept of the true incipiency of lung cancer and elaborate new approaches to its detection in this incipient phase.

These new approaches should be based on the working principle that cancer of the lungs must be suspected long before its presence is indicated by history, symptoms and signs. Clinical experience has amply proved the value of studied overinterpretation of history, clinical symptoms and signs, roentgen features, bronchoscopic and cytologic evidence. By such overinterpretation we must learn how to suspect an ever increasing proportion of potential cases which are to be subjected to a special screening process for the early diagnosis.

This screening process must be further refined with two immediate goals in view;

(1) Detecting growth of the smallest possible extent in the lung parenchyma or in the bronchial mucosa.

(2) Obtaining the earliest possible evidence of conversion from normal to malignant cytologic changes.

Towards these we must move by elaboration of ever more refined methods and technics of roentgenography, bronchoendoscopy and microscopy. These procedures must become widely available and easy to apply.

Regarding the first, the following facts are of special significance. It now appears that large numbers of lung cancers begin in the branch bronchi within the parenchyma of the lungs. Many of these arise far enough in the periphery of the lung to become visible at an early stage as a small opacity. This appears frequently as an umbilicated nodule which becomes visible when it is about 3 mm. in diameter (Ref. Rigler). Sometimes these nodules obstruct a branch bronchus and produce an isolated area of obstructive emphysema in the periphery of the lungs. New growths near and in the root of the lungs may also be suspected early by hilar assymetry, and irregularity of the hilar shadow on the affected side. There is required a most careful scrutiny practically tantamount to an

"over-interpretation of films," with successive frequently repeated x-ray film follow-ups, using planigraphic and special projection technics, focussing directly on the suspected area and the suspected abnormality or irregularity.

With regard to our second goal of earliest discovery of abnormal cells from the bronchi we must aim now to improve our methods of investigation in two directions:

(a) We must elaborate practical methods of bronchial irrigations which can be aimed at the segmental bronchi in that part of the lungs in which the presence of malignancy is suspected. Bronchial lavage must become simple and not too unpleasant to perform so that it may be repeated as often as needed. Aspiration of bronchial contents should become as common a procedure in the future as is now aspiration of fasting gastric contents, in search of tubercle bacilli.

(b) It should now become the urgent task of pathologists to elaborate standardized methods of processing specimens obtained from repeated bronchial lavage and sputa, and to train a large number of personnel in this practice. Stations for the efficient and expeditious processing and interpretation of aspirated bronchial contents should become as widespread as are now stations in our municipal laboratories for processing specimens for diagnosis of tuberculosis.* In the latter, refinement of diagnosis progressed from smear to concentrate, to culture. For analogous progress in the cancer problem, we must now depend on our pathologists to produce the most efficient methods of processing and interpreting the crucial specimens in our continued search for incipient cancer. The earliest evidence of conversion from normal to abnormal exfoliative cytologic findings should become the aim. This should include differential diagnosis of benign metaplasia and cancer-in-situ from true cancer.

The campaign for more and earlier diagnosis will depend greatly for its success upon the cooperation of general practitioners. They must play the key role in the future fight against lung cancer. Continuous contact with the ageing population puts them in the best position to develop that high index of suspicion which will enable them to make the first screening of potential cases and narrow the search to reasonable proportions. Mass processing of whole population groups as now practiced is apparently not profitable enough. Personal observation of those selected for intensified screening must become the task of all physicians in contact with our ageing population.

Highly trained specialists, clinicians, roentgenologists, bronchoscopists, technicians, and pathologists should then be responsible for the intensified

*The writer was happy to note from a report in the current daily press (*New York Times*, August 23, 1954) that our idea with regard to the need for mass processing of secretions for cytologic evidence of cancer has been anticipated by W. E. Tolles, a physicist in charge of a special project at Airborne Instruments Laboratory. He has elaborated an ingenious high speed electronic optical device called "Cytoanalyzer" based on the Papanicolaou smear technic. It was said about this, that cancer authorities who are acting as advisers and observers hold that progress toward a clinical device for mass cancer detection has demonstrated an excellent possibility for success.

screening and final diagnostic processing along the lines suggested above.

Thoracic surgeons too must continue to play a prominent role not only in the treatment but also in the diagnosis of lung cancer. Indeed, for some time to come exploratory surgery will no doubt continue to remain the last resort for the diagnosis of suspected lung cancer. As our campaign with its double screening process will gain momentum and efficiency it is bound to lead to more and earlier diagnoses in an ever increasing proportion of incipient cases and a progressive decrease in purely exploratory surgery.

The least we can hope for is a reduction of mortality rate to the extent already accomplished in the few truly incipient cases found in current surveys. It has been found that among surgeons the death rate from cancer is only 66 per cent of that in the general population, undoubtedly due to their acquired experience in recognizing the early signs of their own cancer. May we not expect physicians in general to acquire such experience and apply it to their patients?

Edgar Mayer, M.D., F.C.C.P.

The President's Page

Our great concern about cancer of the lung and its recognized high death rate has stimulated many men to study the problem from many angles. The simplest solution to the problem would be for us to find the cause of cancer of the lung and to remove the cause, thereby preventing the development of cancer of the lung. Various agents have been suspected of being the cause of cancer. The conclusions arrived at from extensive observations by many authors have differed widely. Certainly, no agent has been proven beyond a shadow of a doubt to be the positive cause of cancer of the lung. The evidence so far gathered would lead us to look for the cause among: 1) factors inherent within the individual; 2) changes brought about within the individual as a result of environmental influences.

It is not improbable that cancer of the lung may be found to be caused by or as the result of a combination of factors. It may be that we have been blinded by the mass of accumulated evidence and that one day we will recognize the cause staring us in the face. Recent studies concerning cell physiology and the influence of various agents on cell physiology open a wide field for further study. The search for the cause of cancer of the lung must go on.

Meanwhile, the patient with cancer of the lung must be treated. He is an important individual and not a statistic. We must conclude in the light of our present knowledge that if we are to cure cancer of the lung, early diagnosis is imperative. Cancer of the lung may be manifest by a variety of symptoms, physical, x-ray and laboratory findings. As the patient approaches and passes the age of forty years, one should be increasingly conscious of the possibility of cancer of the lung. An historical review of the patient's symptoms combined with various x-ray studies, search of the bronchial secretion for cancer cells and bronchoscopic inspection of the tracheobronchial tree for evidence of anatomical and functional changes is the best approach for the diagnosis of cancer of the lung. Repetition of any or all of the above procedures may be desirable. At times, thoracotomy with direct inspection and palpation with microscopic tissue studies may be necessary to determine a diagnosis.

The public should be given information about cancer of the lung but the awakening of the general practitioners to the consciousness of cancer of the lung as a disease of major importance has been a most important factor in improving the outlook for its early diagnosis.

The treatment of cancer of the lung has advanced through improved techniques and know how to the end that an increasing number of five year survivals have been reported. In general, these have been patients who were treated at a time when their cancer was (early) limited in its extent. Early resection of the involved lung combined with radiation, is our most potent weapon today.

In the light of our present knowledge and until more positive information is obtained, the following resolution adopted by the American College of Chest Physicians at its Annual Meeting in San Francisco, June, 1954, expresses in a concise manner the present situation concerning cancer of the lung:

> The alarming rate of increase of cancer of the lung in the past few decades is of serious concern to the medical profession, but particularly to the chest physicians. Such an increase in the incidence of lung cancer makes it mandatory that every effort be exercised to establish the causative factors that may be responsible.
>
> While many theories have been advanced, further work must be carried out before any single agent or agents can be definitely implicated. Early diagnosis remains our greatest weapon in combatting this disease.
>
> As the result of intensive research, many new methods have been developed to assist the physician in early diagnosis of cancer of the lung. Our most important ally in dealing with this menace is the family physician who sees the patient early in the course of this disease and who makes available the necessary diagnostic techniques.

William A. Hudson

21st ANNUAL MEETING
AMERICAN COLLEGE OF CHEST PHYSICIANS

The program to be presented at the 21st Annual Meeting of the College, at the Ambassador Hotel, Atlantic City, New Jersey, June 2-5, appeared in the March issue of DISEASES OF THE CHEST. A copy of the program has been mailed to every member of the College. If you have not received your copy, an additional one may be obtained by writing to the Executive Offices, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Advance Registration

An advance registration form appears in the program and members who will complete this form and return it to the Executive Offices of the College may save themselves considerable time at the registration desk in Atlantic City.

Hotel Reservations

If you have not as yet reserved a hotel room in Atlantic City, it is important for you to do this at once as many of the desirable hotels will be filled to capacity. A reservation coupon may be found on page XII.

Scientific Program

The Committee on Scientific Program for the 21st Annual Meeting has organized what one prominent chest specialist said to be "the finest and most complete program covering all aspects of chest diseases ever to be presented at a College meeting."

American Medical Association

The 104th Annual Meeting of the American Medical Association will be held in Atlantic City, June 6 through 10. The Section on Diseases of the Chest will meet on Wednesday afternoon, June 8, and all day Thursday, June 9. On Thursday morning there will be a joint session with the Sections on Anesthesiology, General Practice and Obstetrics and Gynecology and on Thursday afternoon there will be a joint session with the Section on Radiology. In addition to these interesting sessions, a number of outstanding scientific exhibits will be shown in the Section on Diseases of the Chest of the American Medical Association.

Convocation

The annual Convocation of the College will take place at the Ambassador Hotel on Saturday, June 4, at 6:00 p.m. Approximately 150 new Fellows of the College will receive their Fellowship certificates and, in addition, Honorary Fellowships will be conferred upon the following eminent physicians:

Dr. Geoffrey Bourne, Physician-in-Chief, Cardiological Department, St. Bartholomew's Hospital, London, England

Dr. Andre Cournand, Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, New York

Dr. George R. Herrmann, Professor of Internal Medicine and Director, Cardiovascular Research Laboratory and Heart Station, University of Texas Medical Branch, Galveston, Texas

Rear Admiral Bartholomew W. Hogan, The Surgeon General, United States Navy, Washington, D. C.

Dr. George F. Lull, Secretary-General Manager, American Medical Association, Chicago, Illinois

Major General Dan C. Ogle, The Surgeon General, United States Air Force, Washington, D. C.

Dr. William A. Hudson, Detroit, President of the College, will award the certificates and the incoming President, Dr. James H. Stygall, Indianapolis, will deliver the Convocation Address. Dr. Donald R. McKay, Buffalo, Chairman of the Board of Regents of the College, will preside at this impressive ceremony. The Convocation will be followed by a social hour, the Annual Presidents' Banquet and dancing.

College Chapter News

ARIZONA CHAPTER

The annual meeting of the Arizona Chapter will be held in conjunction with the meeting of the state medical association in Tucson, May 4-7. The following program will be presented by the Arizona Chapter on the morning of May 7:

"Resection for Pulmonary Diseases"
W. H. Oatway, Jr., Los Angeles, California

"Pathogenesis of Coccidioidomycosis"
Charles E. Smith, San Francisco, California

"Special Problems in Cor Pulmonale"
George C. Griffith, Los Angeles, California

Discussion

ARKANSAS CHAPTER

The Arkansas Chapter was formed at a meeting held in Little Rock on February 24, at the Albert Pike Hotel. Dr. William A. Hudson, President of the College, who maintains a residence at Jasper, Arkansas, was honored by the members of the College in Arkansas at this inaugural meeting. The following officers were elected:

President: D. Harvey Shipp, Little Rock

Secretary-Treasurer: William Paul Gray, Batesville

The first scientific program of the chapter will be presented at Hot Springs on May 29. Dr. William A. Hudson, Detroit, Michigan, will be the guest speaker. He will talk on "How Shall We Handle the Patient with Symptoms of Chest Disease?"

CALIFORNIA CHAPTER

The California Chapter will meet on April 30 at the Sheraton-Palace Hotel, San Francisco, preceding the meeting of the state medical association. The following scientific program will be presented:

2:00 p.m. "New Experimental Surgical Methods for the Correction of Myocardial Ischemia"
Alfred Goldman, S. M. Greenstone, M. Chanin, S. H. Strauss, Myron Prinzmetal, and S. Chang, Los Angeles

"Direct Spatial Vectorcardiography—The Clinical Applications"
Bertram J. Allenstein, Los Angeles

"Problems in Bronchial Drainage"
Allergic—Edward Matzger, San Francisco
Bacterial—Seymour M. Farber, San Francisco
Surgical—Lyman A. Brewer, III, Los Angeles

"Effect of Cortisone on the Irradiation Reaction of the Lung"
Reynold F. Brown, San Francisco

Remarks—Robert R. Newell, San Francisco

Presentation of The Chapter's Annual Award Panel on Tuberculosis

"The Growth of the Tubercle Bacillus"
Sidney Raffel, San Francisco

"The Emergence of Resistance"
Sanford S. Elberg, Ph.D., Berkeley

"Anti-tuberculosis Drugs"
H. Corwin Hinshaw, San Francisco

Questions from the floor

5:30 p.m. Social Hour

OKLAHOMA CHAPTER

The annual meeting of the Oklahoma Chapter will be held at the Mayo Hotel, Tulsa, on May 8, commencing at 1:30 p.m., in conjunction with the meeting of the Oklahoma State Medical Association, May 8-11.

GEORGIA CHAPTER

The annual meeting of the Georgia Chapter will take place at the Bon Air Hotel, Augusta, on May 3. The following program will be presented:

8:30 a.m. "Spontaneous Pneumothorax"
Bedford Davis, Atlanta
Discussion: J. L. Alexander, Savannah
"Mistakes and Surprises in the Care of Chest Diseases"
F. Levering Neely, Atlanta
Discussion: Horace E. Crow, Rome
"Fate of Residual Pulmonary Tuberculous Foci"
George W. Comstock, Columbus, Ohio
"Results of Antimicrobial Therapy of Tuberculosis in Children"
Edith Lincoln, New York, New York
Panel—"Chemotherapy of Tuberculosis"
Moderator: Carl C. Aven, Atlanta
Speakers: Mrs. Shirley Ferebee, Washington, D. C.
C. A. LeMaistre, Atlanta
Raymond F. Corpe, Rome
R. C. Major, Augusta

12:30 Luncheon and business meeting

KANSAS CHAPTER

The Kansas Chapter will hold its annual meeting in Hutchinson, May 5, in conjunction with the state medical association meeting. The chapter will present the following program:

10:00 a.m. "Lipoid Pneumonitis"
Paul H. Wedin, Wichita
"Thoracic Procedures in Infancy and Childhood"
Robert Brooker, Topeka
"Lucite Plombage"
Robert K. Purves, Wichita
"Primary Leiomyoma of the Lungs"
Alfred M. Tocker, Wichita
"Human Infections with a Typical Acid Fast Organism in the Greater Kansas City Area"
Ann Pollak, Kansas City
"Treatment of Pulmonary Emphysema"
L. E. Peckenschneider, Halstead

2:00 p.m. Cardiovascular Section—John Morgan, Emporia, presiding
"Myocardial Infarcation Due to an Overdose of Epinephrine"
Benjamin M. Matassarin, Wichita
"Treatment of Leriche's Syndrome"
Creighton Hardin, Kansas City
"The Physiology of Mitral Stenosis"
Frederick Kittle, Kansas City
"Constrictive Pericarditis"
T. K. Lin, Kansas City
"Intravenous Reserpine in the Treatment of Hypertension"
E. Grey Dimond, Kansas City
X-ray Conference
Moderator: Martin Fitzpatrick, Kansas City
Speakers: Newman C. Nash, Wichita
John R. Kline, Wichita
Homer Hiebert, Topeka

6:00 p.m. Social Hour

7:00 p.m. Dinner and election of officers
Guest speaker—Alfred Goldman, St. Louis, Missouri,
Regent, American College of Chest Physicians

ILLINOIS CHAPTER

The Illinois Chapter will hold its annual meeting at the Sherman Hotel, Chicago, in conjunction with the annual meeting of the Illinois State Medical Society, May 17-20. The following program will be presented on May 18:

9:15 a.m. Panel Discussions

"Home Care or Institutional Care of Pulmonary Tuberculosis?"
Abel Froman, Chicago
Robert Levitt, Chicago
M. R. Lichtenstein, Chicago

"Recent Experiences in Diagnosis and Treatment of Cardiovascular Disease"
Benjamin M. Gasul, Chicago, Moderator
Egbert H. Fell, Chicago
Robert F. Dillon, Chicago
Carl J. Marienfeld, Chicago

12:00 noon Luncheon and business meeting

MICHIGAN CHAPTER

At a business meeting at the Detroit Chest and General Hospital on February 16, the Michigan Chapter elected the following officers:

President:	William H. Marrow, Detroit
Vice-President:	Kenneth A. Wood, Detroit
Secretary-Treasurer:	W. Leonard Howard, Northville

A special meeting of the chapter will be held on May 13 at 8:30 p.m. in the Auditorium of the Henry Ford Hospital, Detroit, at which Doctor Richard R. Trial, London, England, Governor of the College and Director of the Papworth Village Settlement in Cambridge, will speak on "Modern Therapy and Rehabilitation in Tuberculosis." Prior to the meeting, there will be a dinner at the Wayne County Medical Society.

MINNESOTA CHAPTER

The Minnesota Chapter will hold a luncheon meeting on May 23 in Minneapolis in conjunction with the state medical association meeting.

MISSISSIPPI CHAPTER

The Mississippi Chapter will meet at the Buena-Vista Hotel, Biloxi, May 9, at the time of the meeting of the state medical society. Dr. Robert E. Schwartz, Hattiesburg, Governor of the College for Mississippi and President of the chapter, will give the opening address, to be followed by a scientific program which will include the presentation of interesting cases by the following chapter members:

Helen Cannon Bernfield, Jackson
Ray H. Biggs, Sanatorium
Henry Boswell, Sanatorium
J. C. Mulhern, Sanatorium
Eugene M. Murphey, Tupelo
Rush E. Netterville, Jackson
Lee R. Reid, Jackson
E. P. Robbins, Brookhaven
William H. Rosenblatt, Jackson
John C. Russel, Cleveland
Hans K. Stauss, Jackson
Matts Webb, Sanatorium

Each case presentation will be followed by a discussion. A social hour will be held at the close of the scientific meeting.

NEW YORK CHAPTER

The annual dinner meeting and election of officers of the New York State Chapter will be held at the Hotel Statler, Buffalo, May 12. The Fifth Howard Lilienthal Lecture will be given by Dr. James Herbert Donnelly of Buffalo. The dinner will be given in honor of Dr. Donnelly's 80th birthday.

PERUVIAN CHAPTER

The Peruvian Chapter held its 8th Annual Meeting in Lima, February 9-11. Following the three-day scientific program, Dr. Ovidio Garcia-Rosell gave a report on the Third International Congress of the College held in Barcelona, October 4-8, 1954. The following members of the College participated in the program: Drs. Ramon Vallenas, Alejandro Flores D., Mario Pastor, Juan Escudero Villar, Max Espinoza Gallarza, Victor Narvaez, Leopoldo Molinari, Carlos Peschiera, Hector Laos E., Marino Molina and Ramon Vargas Machuca.

TEXAS CHAPTER

The Texas Chapter will hold its annual meeting at the Texas Hotel, Fort Worth, April 24, immediately preceding the meeting of the state medical association. The following program will be presented:

9:00 a.m. Registration

9:30 a.m. Symposium: Extra-Pulmonary Tuberculosis
"Tuberculosis of the Vertebrae"
G. W. N. Eggers, Galveston
"Tuberculosis of the Genito-Urinary Tract"
Michael K. O'Heeron, Houston
"Tuberculous Lymphadenitis"
James German, McKinney
"Present Day Treatment of Tuberculous Meningitis in Adults"
I. Horowitz, Kerrville

12:00 noon Luncheon and Business Meeting
"Mechanical Methods of Evaluation of Bronchodilators"
Hollis G. Boren, Houston
Discussor: William F. Miller, Dallas

2:40 p.m. "Diagnosis and Treatment of Fungus Diseases of the Lungs"
David T. Smith, Durham, North Carolina
"The Radiotherapist's View of Lung Cancer"
Vincent P. Collins, Houston
"Medical Treatment of Carcinoma of the Lung"
Warren W. Moorman, Fort Worth

WISCONSIN CHAPTER

The annual meeting of the Wisconsin Chapter will be held at the Schroeder Hotel, Milwaukee, May 1. Mr. Murray Kornfeld, Executive Director of the College, will address the luncheon meeting of the chapter. He will talk on "The Current Program and Future Plans of the American College of Chest Physicians." This will be followed by the business meeting of the chapter and the presentation of the following scientific program:

"Clinical Aspects of Pleurisy with Effusion"
Jay Arthur Myers, Minneapolis, Minnesota
"The Prognosis of Bronchiectasis"
Arthur M. Olsen, Rochester, Minnesota
"The Appraisal of the Routine Treatment of Bronchial Asthma"
George L. Waldboldt, Detroit, Michigan
"Rheumatic Heart Disease is Preventable"
Chester M. Kurtz, Madison
"Therapeutic Implications of Pulmonary Function Studies"
Albert H. Andrews, Jr., Chicago, Illinois
"Advantages Derived from Routine Chest X-ray Examination in a General Hospital"
Abraham Melamed, Milwaukee

PHILIPPINE CHAPTER

The Philippine Chapter presented a special scientific program in honor of Dr. Ovidio Garcia-Rosell, Regent of the College for Peru, at the Quezon Institute, December 7. Dr. Cirilo Santos, President of the Philippine Chapter, presided at the meeting which was opened with brief remarks by Dr. Gonzalo F. Austria. Dr. Enrique Garcia presented a paper on "A Case of Bilateral Giant Pulmonary Cysts (Buerger's Disease) Treated Surgically" which was discussed by Drs. Cristino Lazatin and Carmelo P. Jacinto. Dr. Miguel Canizares, Regent of the College for the Philippines and Director of the Quezon Institute, presented Dr. Garcia-Rosell who addressed the meeting.

The chapter elected the following officers:

President:	Cirilo Santos, San Juan
President-Elect:	Laureano Diaz Bautista, Quezon City
Vice-President:	Leroy K. Young, Manila
Secretary-Treasurer:	Priscilla de Jesus Tablan, Quezon City

HONG KONG AND CHINA CHAPTER

First row (left to right), Drs. Li Shu-Pui, Yew Hong-Ping, Sister Mary Aquinas, Kenneth Hui (Vice-President), Li Shu-Fan (President), S. D. Sturton (Secretary), K. A. Goh, and Look Mang-Wai. Second row, Drs. T. M. Tso, R. T. Eng, T. J. Hua, Chiu Lan-Cheong, S. M. Bard, Tseung Ying-Kay, S. S. Kwan, H. C. Chan.

The inaugural meeting of the Hong Kong and China Chapter was held on February 14 at the Hong Kong Sanatorium and Hospital. Dr. Li Shu-Fan, Governor of the College for China, presided at the meeting which was attended by 15 of the 20 members in the area. The following officers were elected:

President:	Li Shu-Fan, Hong Kong
Vice-President:	Kenneth Hui, Hong Kong
Secretary-Treasurer:	S. D. Sturton, Hong Kong

QUEBEC CHAPTER

The Quebec Chapter will participate in the Fourth Postgraduate Course on Diseases of the Chest, sponsored by the Provincial Committee for the Prevention of Tuberculosis, to be held at the Hopital Laval, Quebec City, Canada, May 5, 6 and 7. The committee for the course is composed of Dr. Alphonse L'Esperance, Chairman, Dr. Philippe Landry and Dr. B. Guy Begin, Fellows of the College, and Drs. Maurice Beaulieu and Lionel Montminy.

Dr. William A. Hudson, Detroit, Michigan, President of the College, will be the guest speaker at a luncheon meeting on Friday, May 6. On the afternoon of May 6, the First Archibald, Dube, Rousseau Memorial Lectures, presented under the auspices of the Quebec Chapter of the College, will be given. Dr. Hudson will present the Edward Archibald Lecture, Dr. J. A. Vidal the Edmond Dube Lecture, and Dr. Renaud Lemieux the Arthur Rousseau Lecture.

A number of Fellows of the College in the Province of Quebec will lecture in the postgraduate course which will cover all aspects of the diagnosis and treatment of tuberculosis and other pulmonary diseases.

On February 25, a joint meeting of the Montreal Medico-Chirurgical Society and the Societe de Phtisiologie de Montreal, sponsored by the Quebec Chapter, was held at the Royal Edward Laurentian Hospital, Montreal. Dr. F. L. Phelps, President of the chapter, served as chairman and a panel discussion on "Treatment of Inoperable Cancer of the Lung" was presented. Dr. B. Guy Begin, Governor of the College for Quebec, served as moderator of the discussion.

JAPANESE CHAPTER

Members of the Japanese Chapter of the College receive Fellowship certificates at meeting held in Tokyo on February 5.

The mid-winter meeting of the Japanese Chapter was held in Tokyo on February 5, attended by more than 150 physicians. The following scientific program was presented:

"Impressions of International Congresses on Chest Diseases in Europe"
Shinnosuke Fujita, Tokyo

"Pulmonary Resection Therapy in Tuberculosis of the Lung"
Ichiro Akakura, Kanagawa

"Present Status of Things Medical in Formosa"
Kingo Shinoi, Tokyo

"Some Considerations Concerning X-ray Diagnosis of Pulmonary Tuberculosis"
Harumichi Oka, Tokyo

Following the scientific program, certificates of Fellowship were presented to newly elected Fellows of the College. The following officers were elected to the chapter for 1955:

President:	Harumicho Oka, Tokyo
Vice-President:	Jiro Ishida, Tokyo
Secretary-Treasurer:	Shinnosuke Fujita, Tokyo

ISRAELI CHAPTER

The Israeli Chapter met at the Raanana Sanatorium, Raanana, December 15. Following the scientific program, the chapter elected the following officers:

President:	Joseph Weiser, Ramat-Gan
President Elect:	Kurt Friedman, TelAviv
Treasurer:	Wilhelm Hupert, Ramatajim

URUGUAY CHAPTER

The Uruguay Chapter held its annual meeting in Montevideo on December 29. Dr. Felix Leborgne presented a motion picture on "Radioactive Isotopes." The following officers were elected:

President:	Aristeo A. Piaggio, Montevideo
Secretary-Treasurer:	Juan Carlos Dighiero, Montevideo

ANNOUNCEMENT

The Committee on Cardiovascular Diseases of the Council on Research, American College of Chest Physicians, announces an award of $500 for the best manuscript on "Acute Pulmonary Edema"—experimental or clinical studies. It must be an unpublished manuscript based on original research.

For further information, please communicate with Dr. Aldo A. Luisada, Chairman, Section on Cardiovascular Physiology, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

MEDICAL SERVICE BUREAU

Position Wanted

Position wanted in field of tuberculosis, any capacity. On staff of large sanatorium since 1938: chief, medical service '41-'44; assistant superintendent since '44. Nearing retirement on reaching statutory age limit of 70. Native American, active, in good health, no dependents. Position and pay secondary. Address John M. Stanley, Assistant Superintendent, Glenn Dale Hospital, Glenn Dale, Maryland.

Positions Available

Resident physician wanted for 160 bed tuberculosis hospital in pleasant rural setting. Available July 1. All medical and surgical therapy utilized. Salary range $325 to $425 plus partial maintenance for family. Tuberculosis experience desirable but not essential. California license mandatory. Apply to Medical Director, Stony Brook Retreat, Keene, California.

Staff physician wanted for 160 bed tuberculosis hospital in pleasant rural setting. Available July 1. All medical and surgical therapy utilized. Salary range $581 to $707 plus partial maintenance for family. Tuberculosis experience desirable but not essential. California license mandatory. Apply to Medical Director, Stony Brook Retreat, Keene, California.

CALENDAR OF EVENTS

21st Annual Meeting, American College of Chest Physicians
Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1955

Fourth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Cologne, Germany, August 19-23, 1956

CHAPTER MEETINGS

New Jersey Chapter, Atlantic City, April 18
Alabama Chapter, Montgomery, April 20
Ohio Chapter, Cincinnati, April 20
Texas Chapter, Fort Worth, April 24
California Chapter, San Francisco, April 30
Wisconsin Chapter, Milwaukee, May 1
Georgia Chapter, Augusta, May 3
Kansas Chapter, Hutchinson, May 5
Quebec Chapter, Quebec City, May 6
Arizona Chapter, Tucson, May 7
Oklahoma Chapter, Tulsa, May 8
Mississippi Chapter, Biloxi, May 9
New York State Chapter, Buffalo, May 12
Michigan Chapter, Detroit, May 13
Illinois Chapter, Chicago, May 18
Minnesota Chapter, Minneapolis, May 23
Arkansas Chapter, Hot Springs, May 29

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Anesthetic Solution and Jelly

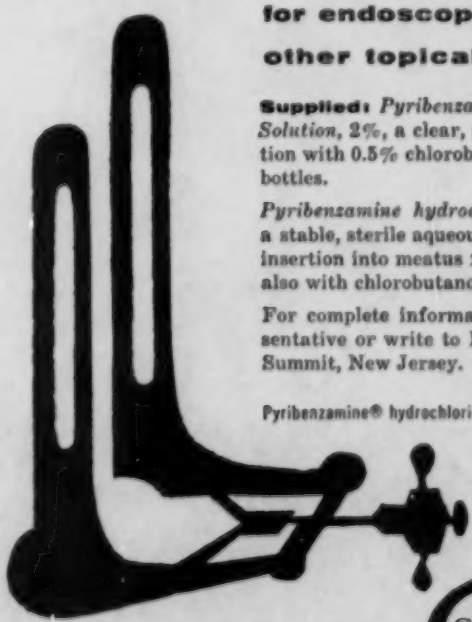
for endoscopic procedures and other topical anesthetic uses

Supplied: *Pyribenzamine hydrochloride Anesthetic Solution*, 2%, a clear, nonviscous, stable, sterile solution with 0.5% chlorobutanol as preservative; in 1-oz. bottles.

Pyribenzamine hydrochloride Anesthetic Jelly, 2%, a stable, sterile aqueous jelly with applicator tip (for insertion into meatus for intra-urethral instillation), also with chlorobutanol; in 1-oz. tubes.

For complete information, consult your CIBA representative or write to Medical Service Division, CIBA, Summit, New Jersey.

Pyribenzamine® hydrochloride (tripelennamine hydrochloride CIBA)



C I B A Summit, N. J.

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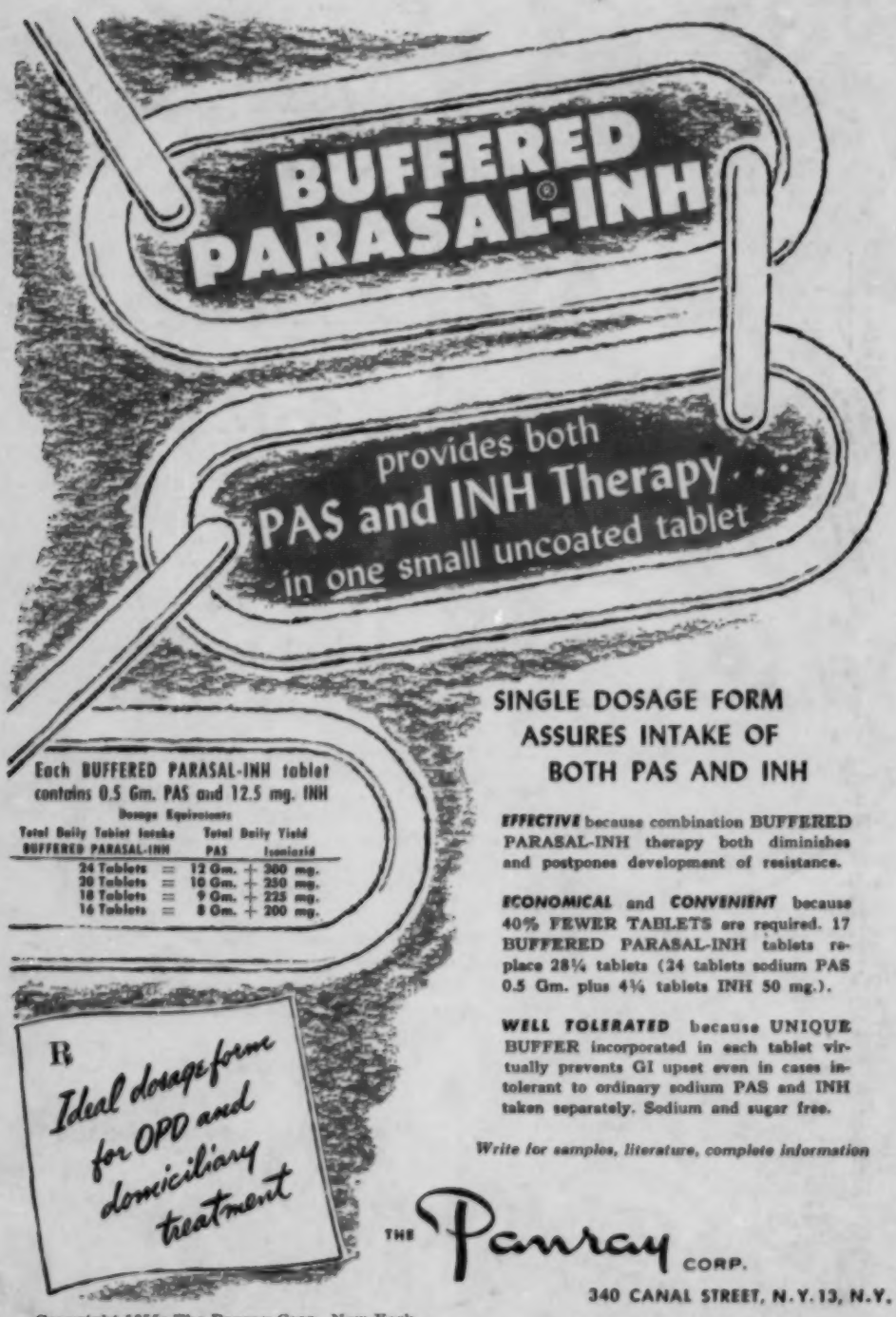

Each BUFFERED PARASAL-INH tablet contains 0.5 Gm. PAS and 12.5 mg. INH

Dosage Equivalents

Total Daily Tablet Intake BUFFERED PARASAL-INH		Total Daily Yield PAS		Isoniazid
24 Tablets	=	12 Gm.	+	300 mg.
20 Tablets	=	10 Gm.	+	250 mg.
18 Tablets	=	9 Gm.	+	225 mg.
16 Tablets	=	8 Gm.	+	200 mg.

℞ *Ideal dosage forms for OPD and domiciliary treatment*

SINGLE DOSAGE FORM ASSURES INTAKE OF BOTH PAS AND INH

EFFECTIVE because combination BUFFERED PARASAL-INH therapy both diminishes and postpones development of resistance.

ECONOMICAL and ***CONVENIENT*** because 40% FEWER TABLETS are required. 17 BUFFERED PARASAL-INH tablets replace 28¼ tablets (24 tablets sodium PAS 0.5 Gm. plus 4¼ tablets INH 50 mg.).

WELL TOLERATED because UNIQUE BUFFER incorporated in each tablet virtually prevents GI upset even in cases intolerant to ordinary sodium PAS and INH taken separately. Sodium and sugar free.

Write for samples, literature, complete information

THE Panray CORP.

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